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THE ARTHRITIC DISEASES AND THEIR TREATMENT.[1]

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To the lay mind the term arthritis conjures up visions of a cripple in a wheel-chair suffering a lifetime of pain. To the doctor consulted by a patient suffering from arthritis come thoughts of laborious and possibly futile treatment. Both are in their own way preoccupied with ideas of an unfavourable prognosis. The picture is not really as gloomy as either may think. If it is remembered that it is only the small minority of patients who suffer from the severe and potentially disabling forms of arthritis, whereas the great majority of people have the condition either in a mild form or not at all, a much truer picture emerges. If the doctor will take the trouble to make an accurate diagnosis and then apply the appropriate form of management, the vast majority of patients in this category can lead a useful and full life. Although it is quite true that the cause of many of the arthritic diseases is unknown and treatment is often empirical, the diligent application of the methods of treatment in use today will control all but the most severe forms.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on October 29, 1955, at Wagga Wagga.

For practical purposes we may group the cases presenting as "arthritis" into the following three categories:

1. Common arthritic diseases; rheumatoid arthritis; osteoarthritis; ankylosing spondylitis; gout.

2. Common *conditions which may present* as "arthritis": non-articular rheumatism; joint or referred pain secondary to trauma, postural strain or visceral disease; periarthritis of the shoulder (painful or frozen shoulder); psychogenic rheumatism.

3. Rare diseases in which arthritic manifestations occur: neuropathic joint disease (*Charcot's joints*); hæmophilia; the "collagen diseases" (disseminated *lupus erythematosus et cetera*); *osteochondritis dissecans.*

I propose to confine the discussion to the first two groups, and to concentrate mainly on the practical problems of diagnosis and treatment. *It is most important* to take a full and careful history and to make a thorough *physical examination, not only* of the joints but of every system. Apart from the more obvious traps, I have recently seen two patients with thyrotoxicosis and a patient with peroneal muscular atrophy who came along complaining of "arthritis". This emphasis on clinical *examination is important* also when one considers the contribution which can reasonably be expected from laboratory aids to diagnosis. In gout, the radiographer can find no changes until the disease has advanced to the stage of chronic tophaceous deposits. The biochemist may find the *uric acid level* in the blood to be within normal limits, while patients suffering from undoubted rheumatoid arthritis may have a raised blood uric acid level. The

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osteophytes almost universally seen in X-ray films of the spine of middle-aged patients are often symptomless, and when there is pain in the back they may not be the explanation of it.

In other cases an X-ray examination may be of great diagnostic importance. The early recognition of sacro-iliac arthritis in the young man complaining of debility and slight backache will allow the diagnosis of ankylosing spondylitis to be made long before clinically recognizable features of the disease are present. Secondary neoplastic deposits may be seen and prevent futile treatment for "arthritis".

For these reasons, do not neglect the laboratory investigation of the patient, but interpret the results in the light of the complete clinical picture.

NON-ARTHRITIC CONDITIONS.

Two of the non-arthritic conditions mentioned above merit special discussion.

The Painful Shoulder.

The painful shoulder is a common condition of uncertain and variable ætiology. It should not be confused with the shoulder lesions of rheumatoid arthritis, which are commonly bilateral and associated with lesions of other joints, such as hands, wrists and knees. The primary lesion may occur in the subacromial bursa, in the supraspinatus tendon or in the "rotator cuff". The main consequence is a prolonged restriction of movement of the shoulder by secondary contraction of the lower part of the capsule of the shoulder joint, accompanied by pain and showing no spontaneous tendency to recovery. In long-standing cases there may be wasting of the deltoid muscle simulating that seen in progressive muscular atrophy.

The treatment includes general measures to relieve pain and ensure sleep; but most important is the programme of local treatment. Exercises and assisted (almost forced) movements are essential, but tend to provoke or aggravate pain unless associated with some local pain-relieving treatment. In the early stage this may be by injection of procaine into the bursa or in the region of the tendon. The application of heat in the form of short-wave diathermy may help. However, the most effective local measure is the injection by the anterior approach into the shoulder joint of hydrocortisone acetate suspension in doses of 1·0 to 1·5 millilitres. This may be repeated at intervals of seven days for as long as is necessary. In recent cases one or two injections will suffice. In long-standing cases many injections may be necessary. Manipulation of the shoulder will secure a full range of movement, but the after-care must be meticulous. The intra-articular injection of hydrocortisone may reduce the pain; but the capsule will contract again unless the shoulder is put through full-range exercises several times daily for many weeks.

Psychogenic Rheumatism.

In true psychogenic rheumatism there is a psychoneurosis with no demonstrable abnormality in the musculoskeletal structures. The patient complains of severe pain, and physical examination reveals no swelling or tenderness of joint structures and no limitation of movement. It should be possible to elicit positive evidence of the psychological basis of the malady in the psychiatric history.

Mrs. A., aged fifty-three years, consulted me on September 9, complaining of generalized aching which involved the neck, spine, knees, ankles, hands and wrists; it had been present for about sixteen years, but had become much worse in the last twelve months. There had been no loss of weight, but she had difficulty in sleeping.

On examination of the patient there was no objective sign of joint disease, but she was a tense, anxious person. Further interrogation revealed that she and her husband had recently moved into a house on which they had paid a deposit, that she was working part-time at a city store, and that they denied themselves all outings and enjoyment with the object of paying off the house as rapidly as possible. Both she and her husband had a horror of being in debt, and they regarded the debt of the house as a burden which must be discharged before they could allow themselves any recreation.

When the nature of the trouble and the mechanism by which nervous tension could be translated into musculoskeletal pain were explained to her, there was considerable improvement. This improvement was accelerated by the administration of chlorpromazine ("Largactil") in doses of 25 milligrammes thrice daily.

In other cases a psychogenic element may perpetuate the disablement beyond the degree and duration expected. This type of problem is often encountered in cases in which workers' or other compensation is involved. One may speculate on the question of how near the conscious level the psychological factor may be, and in some cases reach the conclusion that it is so close that the term malingerer may fairly be applied. In other cases the mechanism is more obscure and the motivation hard to work out. The treatment is very difficult. Possibly the wider use of rehabilitation centres may help to solve the problem.

The third aspect of the relation of psyche and soma in the field of arthritic disease is the interplay of organic disease with pain susceptibility. It is my impression that the sufferer from severe arthritis is a patient person who endures great discomfort with fortitude and makes a prodigious effort to overcome a major disablement. This is just as well, as the conquest of the disease often requires from the patient whole-hearted cooperation in a rather prolonged and strenuous programme. It is important for the clinician to know the strengths and weaknesses of the patient's character, for he is then equipped to develop in him those inner resources which will play a large part in successful treatment.

RHEUMATOID ARTHRITIS.

Rheumatoid arthritis is a constitutional disease which may occur in all degrees of severity. Its cause is unknown, and no form of treatment has yet been devised which can be called a cure. Left to itself, it may eventually burn itself out, leaving a variable degree of destruction in its wake. However, far more mild than severe forms occur, and the various methods of management can offer the majority of patients adequate even if not perfect control of the process. Each patient presents an individual problem calling for a choice of therapeutic weapons best suited to the needs of the moment. The clinician has abundant opportunity to demonstrate his resourcefulness when he pits his skill against this treacherous enemy. The factors considered in the planning of treatment include the stage and degree of activity of the disease, the occupation and sex of the patient, and the functional capacity.

The weapons are as follows: rest, partial or complete; nutrition; hæmatinics; analgesics and hypnotics; local treatment (heat and massage, splints, exercises); special drugs (salicylates, gold, "Butazolidin" *et cetera*); hormones (cortisone, hydrocortisone, ACTH, the newer synthetic steroids—for example, Δ-1-dehydrocortisone); orthopædic treatment (arthrodesis, arthroplasty *et cetera*); rehabilitation (occupational therapy, physical training, splints, crutches and other apparatus, "gadgets" and modifications of household arrangements to facilitate the activities of daily living).

The patient with very severe and rapidly advancing disease requires rest in bed in hospital. Patients with the milder forms require less rigid programmes of rest, but all should have some relief from the full responsibilities of work or household duties. The anæmia of rheumatoid arthritis is of the normocytic, hypochromic type, and responds poorly to the oral administration of iron. Some patients need a blood transfusion. Intravenously administered iron is of benefit to some. When the disease passes into remission, spontaneous relief of the anæmia occurs.

An actively inflamed joint should be splinted. A plaster cast applied to such a joint and left in position for a week or so often brings about considerable reduction of joint pain and swelling. The cast can then be removed and used as a removable splint while the joint is being treated daily by physiotherapy.

Salicylate and Aspirin Therapy.

The administration of sodium salicylate or aspirin serves a twofold purpose. The salicylates possess both analgesic and antirheumatic properties. They have a wide margin of safety. A recent trial by the Medical Research Council in Great Britain showed that the long-term results of aspirin treatment in early active cases compared favourably with the results of cortisone treatment. When the salicylates or aspirin are used, large doses just short of the central toxic effects of tinnitus and deafness should be given.

The actual dose varies for different patients, but is of the order of 60 grains a day. Enteric-coated sodium salicylate tablets are less apt to cause gastric irritation than plain aspirin, and may be better tolerated.

Aspirin may cause local irritation of gastric mucosa with symptoms of heartburn, nausea, epigastric fullness and pain, anorexia and vomiting. Hæmatemesis and melæna have been described arising from aspirin therapy (Hurst *et alii*, 1939). The addition of buffers such as aluminium hydroxide, glycine and magnesium carbonate to the aspirin may reduce the incidence of local intolerance.

The regular administration of phenacetin in combination with aspirin is undesirable for long-term cases, as the phenacetin causes alteration of hæmoglobin to methæmoglobin. Such patients have a blue colour suggesting cyanosis.

The programme of general management combined with prolonged salicylate therapy may be all that is required in some cases of rheumatoid arthritis.

Gold.

Gold was first used in the treatment of rheumatoid arthritis by Lande in 1927, and came into common use after Forestier (1929) had reported favourably on its effects. In spite of considerable uncertainty as to its long-term value, complete ignorance of its mode of action and an appreciable risk of toxic effects, it remains firmly established as a therapeutic agent in most of the rheumatic clinics throughout the world. The toxic effects include damage to bone marrow (leucopenia, agranulocytosis, thrombocytopenic purpura and aplastic anæmia), kidneys (transient albuminuria, toxic nephritis), liver (toxic hepatitis) and skin (toxic erythema, exfoliative dermatitis). Care should therefore be taken to test the urine before each injection, to watch for skin eruptions, and to carry out blood examinations at frequent intervals. The patient should be examined and questioned by the attending physician before each injection. Aqueous "Myocrisin" solution is a satisfactory preparation, given intramuscularly at weekly intervals, the first dose 10 milligrammes, the second 20 milligrammes, and the weekly dose thereafter 50 milligrammes. It may be given in courses of 0·5 to 1·0 gramme with an interval between courses, or preferably the intervals between doses may be extended to two to four weeks after the first 0·5 gramme has been given, the object being to maintain the remission without complete cessation of the treatment. When gold is given in a single course with favourable response there is a tendency for the disease to flare up again three to six months after cessation of therapy. Subsequent courses may not result in such a favourable response.

Toxic manifestations call for immediate cessation of the drug and for the detoxication of retained gold by BAL (2,3 dimercapto-propanol), three milligrammes per kilogram of body weight being given every six hours for three or four days. In skin eruptions the simultaneous administration of cortisone usually results in dramatic relief of the rash. In liver disease BAL may be toxic to the damaged liver, and smaller doses (2·5 milligrammes per kilogram) should be used.

Phenylbutazone ("Butazolidin").

Phenylbutazone ("Butazolidin") is a wide-range drug with selective analgesic effects in the rheumatic group of diseases. It is thought to have in addition a mild anti-inflammatory effect and a definite uricosuric effect. It is capable of causing salt and water retention, and may also cause gastro-intestinal irritation and skin rashes of the morbilliform type.

It is rapidly absorbed and slowly excreted. The effective blood level has been shown by Bruck *et alii* (1954) and Currie (1953) to be 5 to 10 milligrammes per 100 millilitres. This level may be attained by administering a loading dose of 800 milligrammes in divided doses in one day, or 600 milligrammes a day for two days, and may be maintained by the daily administration of 200 to 300 milligrammes a day thereafter.

Toxic effects are mild and infrequent at this low dosage level. No increase in therapeutic efficiency is derived from higher doses while the incidence of toxic effects increases steeply. The proper dose is the smallest that produces therapeutic effect. If no satisfactory response is seen when the drug is given in the recommended doses, it is better to abandon its use than to risk serious toxic effects by raising the dose.

Phenylbutazone is contraindicated for elderly or hypertensive subjects and in severe cardiac disease on account of the increase in blood volume. It is also contraindicated in cases of peptic ulceration. Mild skin eruptions settle down if the drug is suspended, and may not recur if its administration is recommenced.

The most serious and feared complication is agranulocytosis. Deaths were reported when the drug was first introduced, but at this time much higher doses than those now advised were in use. Nevertheless, white cell counts should be made at intervals of one or two weeks during the early stages of therapy and at intervals of four to eight weeks later. The patient should at all times be kept under regular supervision, and told to report any sore throat or other febrile illness.

In rheumatoid arthritis administration of the drug must be prolonged; in favourable cases there is considerable relief of the pain and to a less extent reduction of the swelling around the joints. Suspension of the drug usually results in a prompt return of the symptoms. Little if any alteration of the sedimentation rate of the blood occurs even when the response is favourable, unless the disease passes into remission. "Butazolidin" may be used to supplement cortisone, and this combination may result in a definite economy in the cortisone requirements.

Steroid Therapy.

Cortisone is capable of producing suppression of the active phase of rheumatoid arthritis. The lay Press has in turn lauded it as a "wonder drug" and publicized the unpleasant side-effects. Practitioners are divided into those who perhaps use it too freely and those who denounce it as dangerous. Hench (1954) draws attention to what he calls the "side effects" of rheumatoid arthritis, and shows the picture of a pathetic arthritic cripple.

In sober consideration of its use in a particular case one must think of the disease, the patient, the facilities for treatment and the known facts concerning the effects of the hormone, favourable and unfavourable.

With regard to the disease, in the main its use is considered only in the more severely active forms in which other measures have failed to give adequate relief. In practice this means that cortisone is given to the problem patients who are likely to do badly on any form of treatment. I believe that in such cases it is often responsible for the prevention of severe forms of crippling, even when some progression of the lesions still occurs.

When the factors relating to the patient are considered, the sex, the age, the distribution of the joint lesions and the relation of economic factors to employment are kept in mind. There should also be a review of the patient in respect of the presence of other diseases, such as tuberculosis and peptic ulceration, which would contraindicate the use of cortisone.

If suitable facilities for institutional treatment over a long term were to be available, some patients might be so treated with general measures, administration of aspirin *et cetera*, and not given cortisone at all. Such facilities do

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exist in some overseas centres whose directors claim to avoid cortisone.

The expected favourable effects of the hormone — the anti-inflammatory ones—are well known. In very severe cases these may not be attained at a dosage level considered safe. No alteration in the underlying activity of the disease process is to be expected, and there is often a prompt return to a state which may be worse than the pre-treatment level if the hormone is suspended. The moon-face, striæ, hirsuties and acne are probably of not much danger in themselves. Mineral imbalance—sodium retention and potassium depletion—calls for adjustment of mineral intake, and except in patients with renal disease is no great problem. This effect is minimal when small maintenance doses are given. Because of the anti-inflammatory effects of the hormone, infections or inflammation may be masked. Patients may develop a peptic ulcer and this may rupture with little warning. The adrenal cortex becomes inactive, and recovery of function may be slow. This particularly applies to its capacity to react to stress. Salassa *et alii* (1953) draw attention to the occurrence of post-operative adrenal cortical insufficiency in the subjects of previous cortisone therapy. In such cases it is necessary to give cortisone parenterally pre-operatively and post-operatively, to provide a depot to tide the patient over the period of stress. This precaution probably applies to patients suffering infections as well. If you are called in an emergency to a patient receiving cortisone therapy, do not in a lordly fashion suspend all previous treatment, but make careful inquiry first and adjust the dose to suit the problem.

Current practice is to give cortisone by mouth in four doses spaced through the day. Doses of 150 milligrammes a day are given for the first two days, the dose then being reduced to 100 milligrammes a day for about a week, then lowered by stepwise reductions of 12·5 milligrammes a day until a maintenance dose is reached which produces almost complete suppression of the symptoms. A maintenance dose of 87·5 milligrammes a day is exceeded in rare instances. Therapy is maintained indefinitely. The guide to its cessation is the maintenance of control on ever-decreasing doses, and one must be on the alert to try small reductions from time to time.

Hydrocortisone and ACTH are similarly used. The disadvantage of ACTH is the need for parenteral administration. However, the slowly absorbed forms require a single daily dose and may be more effective in some cases.

The indications for the use of steroid therapy may be summarized as follows: (*a*) severe and progressive disease not responding to other forms of treatment; (*b*) lowering of the patient's working potential in cases in which the use of the steroid may be expected to restore economic usefulness.

Patients whose disease is successfully controlled on cortisone may tend to undertake more activity than is deemed prudent. They should be instructed to restrict activities which are unnecessary, such as sports and hobbies or superfluous housework, as the joints are still capable of being damaged by such stresses even though the more obvious signs of inflammation are suppressed.

New Synthetic Steroids.

Various synthetic products have been under trial in an endeavour to produce a more potent anti-inflammatory effect with reduced side-effects. One, containing fluorine (9-α-fluoro-hydrocortisone), was a failure, as the mineral-retaining effects were increased disproportionately. Two products resembling cortisone and hydrocortisone respectively except for a double bond in the first ring between carbons 1 and 2 have been released under various trade names. As "Metacortandralone" and "Metacortandracin" they were tried by Bunim and his co-workers at the National Institute of Arthritis and Metabolic Diseases in Bethesda, Maryland, late in 1954. I have had a quantity of δ-1-dehydrocortisone made available to me for clinical trial by Merck and Company. In 14 cases this has proved a satisfactory anti-inflammatory agent. Nine patients have been transferred from maintenance doses of cortisone to the new steroid by the abrupt substitution of one tablet of five milligrammes of δ-1-dehydrocortisone for each 25-milligramme tablet of cortisone. No signs of adrenal cortical insufficiency have been noted. The anti-inflammatory action of the new substance is equal or superior to that of cortisone on this basis of substitution. Some patients report reduction of subjective feelings of tension. Signs of mineral imbalance have not occurred. One patient had a surgical operation without delay in healing.

In the five new cases the starting dose was 15 milligrammes a day, which produced adequate suppression of the joint symptoms and signs.

This constitutes a preliminary report on periods of observation not exceeding eight weeks. A more detailed report is in process of preparation.

Intraarticular Injection of Hydrocortisone.

It is possible to accelerate the suppression of inflammation in certain joints by the injection of small quantities of hydrocortisone acetate suspension into the joints. The dose ranges from 12·5 milligrammes (0·5 millilitre) in the case of small joints to 50 milligrammes (two millilitres) in the large joints. With very careful asepsis this can be carried out as an office procedure. Aspiration of any fluid in the joint is a necessary preliminary to the injection. There is a special approach for each joint.

Rehabilitation.

Under the general heading of rehabilitation come all those measures designed to restore the patient to useful functional capacity. Occupational therapy and physical training play a part in this aspect of treatment—likewise splints, crutches and other apparatus. In overseas clinics one sees on display an impressive array of gadgets ranging from simple to complex, which may enable the patient to make use of damaged limbs and joints for the activities of daily living. Large-diameter handles for knives and forks, additional leverage on taps, doors and keys, raised seats on the lavatory pan, and the placement of grips and handles at strategic points around the house are examples of the application of simple, common-sense principles to the problems involved. Once the idea is given to the patient, the family handyman can often make life much easier and increase the range of useful activity of the arthritic cripple. Modifications in the height of the stove and in the placement of electric switches, and other changes in the kitchen may allow the arthritic housewife to carry out many domestic tasks thought beyond her power. These matters are just as much part of the management of rheumatoid arthritis as the choice of drug.

Treatment of Osteoarthritis.

The following present typical problems in the treatment of osteoarthritis: (i) osteoarthritis of the hands, (ii) osteoarthritis of the knees, (iii) osteoarthritis of the hip, (iv) osteoarthritis of the cervical part of the spine, (v) osteoarthritis of the thoracic and lumbar parts of the spine.

Hands.

Heberden's painful nodules at the terminal interphalangeal joints occur mainly in women and are hereditary. The condition has been well reviewed by Strecher (1955) in the 1954 Heberden Oration. They are painful only at the onset, and may then present as a small bursa containing a glairy fluid over the bony prominence. During this phase a very small (0·1 millilitre) injection of hydrocortisone will give relief. Later development of the node and, in some cases, the subluxation of the joint cannot be prevented. It is disfiguring rather than incapacitating and, at this stage, painless.

More trouble is caused by persistent painful arthritis of the first carpo-metacarpal joint. This is a mobile joint in the hand, and usually the symptoms resist both general treatment and local physiotherapy. The most effective and rapid method of treatment is the intraarticular injection of 0·5 millilitre of hydrocortisone acetate suspension, which may be repeated if the pain recurs. The site of injection

is in the anatomical snuff-box on the ulnar side of the *abductor pollicis longus*, the large superficial veins in the region and the radial artery being avoided. A fine (24 gauge) needle is used.

The proximal interphalangeal joints may also be injected, 0·5 millilitre of the hydrocortisone suspension being used. The needle is inserted tangentially from either side, the joint capsule being perforated under the extensor expansion at the level of the joint.

The most useful way of applying heat to the arthritic hand is by the use of paraffin wax baths. The wax is adjusted by the addition of liquid paraffin to a melting point of 120° F. This form of treatment can be used at home, and needs no other apparatus than a source of heat and a vessel tall enough to accommodate the hand and wrist. When the wax is melted the hand is dipped and removed several times until a glove of wax forms on the hands. The hands are then wrapped in a scarf and left in the wax glove for half an hour before it is peeled off.

Osteoarthritis of the Knees.

Osteoarthritis of the knees is commonly met with in middle-aged women. There may be certain endocrine and metabolic aspects of the general health — obesity, menopausal symptoms, hypothyroidism and hypertension — which merit attention. Analgesics are commonly used (for example, aspirin and salicylates), but these probably have little effect on the local disease. The most effective analgesic is probably "Butazolidin", in the doses recommended for rheumatoid arthritis.

Local treatment includes the application of various forms of heat—infra-red and short-wave diathermy—which may reduce the pain. Histamine ionization is sometimes more effective than short-wave diathermy. The quadriceps muscles are usually weak and atrophic, and improvement in the ability of the patient to negotiate stairs and slopes often follows static contraction exercises. There is, in many cases, a faulty habit of walking which can be improved by instruction from a competent physiotherapist.

Where valgus and varus deformities exist, pain and aggravation of the arthritis are due to the postural defect, and little can be done for this except weight reduction.

The intraarticular injection of hydrocortisone is often most effective. The duration of relief after a single injection varies from a few days to a few weeks, and it is difficult to tell in advance what the response of an individual patient will be. The site for injection is the medial aspect of the joint between patella and femur, and the quantity is 25 to 37·5 milligrammes (1·0 to 1·5 millilitres). Any fluid present should be aspirated prior to the injection. A 20-gauge needle should be used.

The higher esters of hydrocortisone (the tertiary butyl acetate) have been used overseas; they have a more prolonged action than the commonly used acetate.

Osteoarthritis of the Hip (Morbus Coxæ Senilis).

Osteoarthritis of the hip causes both pain and restriction of movement. The pain may sometimes be controlled better by "Butazolidin" than by other analgesics, but many of the sufferers may be too old or hypertensive for this drug to be used safely.

Other measures which may help are short-wave diathermy or, in certain cases, ultrasonic therapy. The latter makes use of a piezo crystal sound-head made to oscillate at a frequency of 80 to 400 kilocycles by passing a high-frequency electric current through it (as in a crystal earpiece of a deaf aid). The resulting sound waves generate heat and possibly create other changes in the tissues.

Pain may be sufficiently intense to warrant surgical intervention (for example, cutting of the obturator nerve) for its relief, but anatomical variation in the obturator nerve may render this operation uncertain.

Relief of pain, by reduction of muscle spasm, will often improve the range of movement. Such movement as is present may be retained or in some cases increased by suitable non-weight-bearing exercises.

Surgical Treatment.

When the limitation of movement is extreme, especially if the joint is fixed in a bad position (for example, flexion adduction), serious consideration is given to surgery. The choice is between arthrodesis and arthroplasty. The advantages of the former are stability in a good position and freedom from pain, but movement is then dependent on the lumbar part of the spine, which may itself be the seat of arthritic change. Vitallium cup arthroplasty is a longer and more difficult operation than the use of an acrylic head prosthesis, but is more durable.

Either operation demands a prolonged convalescence with skilled post-operative supervision of exercises. The results in good hands are excellent, painless joints with a good range (up to 75% of the normal range) being the reward to the patient for a lot of hard work. Patients of robust type, aged less than sixty years, are suitable for operation. They should not be over-persuaded; but the advantages and disadvantages should be put to them clearly and the decision left with them.

Intraarticular Injection of Hydrocortisone.

The hip joint is difficult to inject. The anterior approach is the best, the needle being inserted obliquely backwards and medially from a place lateral to the femoral vessels. The needle should be three inches in length. The usual dose is two millilitres (50 milligrammes) of hydrocortisone acetate suspension. Pain is often considerably relieved by the manœuvre; but about 30% of the attempts to inject the joint may be failures.

Osteoarthritis of the Spine.

In many cases osteoarthritis of the spine is symptomless. The neurologists are aware of the neurological complications of cervical osteoarthritis, which may cause pressure on the cervical part of the cord, thereby producing a syndrome resembling disseminated sclerosis. Here treatment is directed towards the complications rather than towards the main disease. The use of an immobilizing collar of "Perspex", leather or felt is often helpful.

When there are no neurological complications and when the arthritic disease is not too pronounced, neck manipulation and stretching in a Glisson sling may be beneficial. Short-wave diathermy is sometimes useful. Often, in spite of apparent X-ray evidence of cervical osteoarthritis, the origin of the pain is in painful "fibrositic" nodules in the soft tissues of the neck. The use of short-wave diathermy and injection of 1% "Novocain" solution into these nodules will often give relief of symptoms.

Lumbar Osteoarthritis.

When lumbar osteoarthritis is suspected, one must first be sure that the painful back is in fact due to the arthritic changes and not to referred pain, postural strain or fibrositis. Analgesics, including "Butazolidin", short-wave diathermy, and for women suitable corsets with special back supports, are our therapeutic weapons. Sometimes manipulation of the back will help.

The Treatment of Ankylosing Spondylitis.

The main method of treatment of ankylosing spondylitis is by X rays. The dose must be adequate—1200*r* to 1800*r* to the whole of the spine (the sacro-iliac joints and the lumbar, thoracic and cervical regions).

The following are special problems.

1. Ankylosing spondylitis in the young female. In this condition the normal dose of X rays to the sacro-iliac joint would result in destruction of the ovarian tissue with an artificial menopause. Special tangential beam techniques have been developed which leave the ovary more or less unscathed. An occasional minor disturbance of menstrual rhythm is the only untoward result of treatment.

2. Persistent pain after full X-ray treatment. Here "Butazolidin" is probably the most useful drug, with analgesic properties superior to those of other drugs.

3. Arthritis in peripheral joints. Some patients develop acute arthritis in peripheral joints, usually the larger

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joints, such as hips or shoulders. X-ray therapy with a full programme of rest, reeducation and analgesics will usually bring these joints under control.

4. The management of the acutely ill and debilitated patient. Rest is essential. To prevent kyphosis and other back deformities, the patient may require to be nursed on a plaster bed. He may need special diets, rich in vitamins, iron given intravenously or blood transfusion—in fact, all the general measures used for a very sick rheumatoid arthritic.

5. Chest expansion and posture. The chest expansion at the time of diagnosis may be as little as half an inch. By a careful programme of breathing exercises carried out after X-ray therapy this may be increased. The great wasting of back muscles which occurs in the acute phase of this disease demands active exercises of an extensor type after X-ray therapy is complete. This will correct a tendency to kyphosis and protrusion of the neck.

6. The neglected, deformed patient with the disease in a late stage. This is a tragedy of missed diagnosis. Something can sometimes be done to salvage the wreck. If activity is present, pain may be reduced by X-ray therapy even though movement may be permanently lost. In inactive cases, in which the horizon is limited by the eyebrows, a lumbar osteotomy may restore a better posture and enable the patient to lead a more normal life. One of my patients, for whom Dr. L. J. A. Woodland performed this operation, was able to marry.

The Treatment of Gout.

The management of the acute phase of gout is by adequate doses of colchicine. I prefer the alkaloid in doses of $^1/_{120}$ grain at hourly intervals until either relief or diarrhœa occurs. This takes on the average about 10 tablets. When the acute phase is over, a maintenance programme is organized. This consists of restriction of protein intake, prohibition of foods specially rich in nucleoprotein (liver, kidney *et cetera*) and oxalate-containing foods (tomatoes, celery, plums, prunes, rhubarb, strawberries, spinach), with avoidance of alcohol or strict moderation in its ingestion.

Some uricosuric agent (of which "Benemid" in doses of 0·5 gramme three times a day is the most potent) should be taken continuously. "Benemid" and salicylate are antagonistic and should not be taken together. Salicylate in high doses (40 to 60 grains a day) is an alternative to "Benemid" (and not as expensive).

The administration of "Butazolidin" in doses of 800 milligrammes daily for two days, 600 milligrammes daily for two days, and 300 milligrammes daily for a week is a valuable method of treating the subacute attack, or the attack which has passed unrecognized for a week or two. It is in such cases that colchicine fails to give satisfactory results.

The use of hydrocortisone by intraarticular injection is frequently helpful in both the acute and subacute attack. The relief is often dramatic.

Cortisone given by mouth is disappointing. While the attack may subside shortly after treatment is commenced, another joint frequently flares up while the patient is still taking the hormone. This will require treatment by "Butazolidin" or colchicine.

Some instability of the gouty state may arise at the beginning of treatment by "Benemid". This may be overcome by the use of larger doses, up to three grammes a day, or by alternating "Benemid" and "Butazolidin". Some patients appear to do better on "Butazolidin" in continuous low dosage.

Summary and Conclusions.

I have reviewed the common problems in the diagnosis and treatment of the arthritic diseases. One needs to be on guard against the facile assumption that a patient who appears to have arthritis is in fact a true arthritic, even if X-ray evidence appears to support that diagnosis. In the words of W. S. Gilbert:

> Things are seldom what they seem.
> Skim milk masquerades as cream!

If he (or she) is in fact suffering from arthritis, it is probable that the intelligent application of the known methods of treatment will so modify and relieve the disease that the outcome will be favourable to the patient. Even the unhappy minority of patients who have severe and potentially crippling disease can derive much benefit from modern techniques of treatment. However, the more potent agents carry their own risks, and need to be used with restraint and with a sense of responsibility.

The many problems with which our arthritic patients confront us are a challenge to our therapeutic resourcefulness and are reminiscent of the once encountered challenge of typhoid fever and pneumonia. Pending the discovery of a specific cure, may we meet them with the same skill and enterprise.

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SURGERY OF HAND TRAUMA.[1]

By P. H. Greenwell, F.R.C.S. (England),
Sydney.

I wish to express my appreciation of the opportunity to speak on the all-important subject of the surgery of hand trauma. It is my belief that until more recent times we have not given due regard to the management of the injured hand. It is therefore pleasing that the subject has been considered worthy of a place in this week-end's discussions.

Granted, hand injury seldom if ever jeopardizes life itself, but its economic and social significance is extreme. Injury to the hand may render a breadwinner incapable of maintaining his dependants, and equally prevent a skilled technician from giving service to his calling.

The hand, by virtue of its prehensile and perceptive purpose, is highly vulnerable. Even so, it is surprising to reflect upon the fact that one-third of all injuries at the casualty department of a major hospital are of this nature. Industry and the home sphere provide 90% of these injuries, and less than 10% are the result of vehicular accident, which is regarded as a common source of injury elsewhere in the body.

The management of the injured hand should be discussed under the following two specific headings: (*a*) primary treatment—that rendered in the first instance; (*b*) secondary treatment—that treatment, both surgical and physiotherapeutic, which is concerned with the established sequelæ, the deformities, and the late repair of deep structures.

Experience has taught that a satisfactory outcome in these cases is dependent upon the correct application of the principles of primary repair. It is for this reason, and because of the fact that our common concern lies herein, that these principles will constitute the material of this lecture.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on October 29, 1955, at Wagga Wagga.

PRINCIPLES OF TREATMENT.

Examination and Assessment.

Examination and assessment should be carried out along the following lines.

History.

Injury is often self-explanatory, and the patient's own account or that of an eye witness may not assist to any great extent in its appreciation. However, in some cases details of accident may bring some understanding, and they are at all times of considerable interest. In certain circumstances such details may be more than interesting, they may be vital to the management. The knowledge of the agent in a case of hand burning by corrosive may lead to the timely application of a suitable neutralizing agent. Violence of a compression type may bring appreciation or suspicion of deep avascular damage and will direct treatment of the soft tissue injury. A record of the time and date of injury is, of course, essential. The time relationship between occurrence and effective measures may dictate the approach. For example, the decision as to primary closure of a wound may depend in part on this knowledge.

Physical Examination.

Far more important than the history is the thorough and organized examination of the hand. In practice, this is conducted at two specific times, as follows: (i) A preliminary pre-operative examination is carried out in the surgery or casualty department. This examination is mainly concerned with an appreciation of function. (ii) A detailed examination of the injury is carried out at operation, and is concerned with a determination of the physical damage.

The first examination takes little account of the wound itself, for it is judged inadvisable to probe and search the wound at this time. The operator should, with mask protection, merely observe the extent of the damage, thus making a quick visual appreciation upon which reflection may later suggest the possibilities of the damage which underlie the superficial breach. The posture of the hand or finger, the inability to perform an individual movement, the lack of natural tension, may determine tendon involvement or severance. Sensory changes or loss of motor capacity of the small musculature of the hand may bring suspicion of nerve damage. Finally, X-ray examination will disclose problems relating to the bony structures and define radio-opaque foreign body material, which may be concerned with the injury.

At operation, and only then, should the second examination be made, when opportunity for close perusal of the wound is given.

Anæsthesia.

In general terms hand surgery demands a general anæsthetic. There is no place for inefficient anæsthesia—the "freeze" of ethyl chloride, the "controlled anoxia" of nitrous oxide anæsthesia, are and should be things of the past. There is a place for local block techniques in experienced hands, but infiltration of local agents is short-lived and inefficient.

The standard "open ether" technique is admirable for this work, even in this era of closed circuit methods combining multiple agents.

Preparation of the Operation Area.

To Sumner Koch must be given much credit for the present concept of wound toilet. It is fair to say that the greatest single factor in satisfactory wound healing is the correct application of wound cleansing. With sterile gloves and the injured hand resting in a sterile tray, cleansing with gauze squares is carried out, soap or other detergent agent being used. Time is consumed in this procedure, but this must not be considered. Cleansing continues till the skin and the wound edges are thoroughly clean, and then they are prepared with suitable lotion.

With regard to the wound itself, foreign body material and blood clot are picked out and the cavity is irrigated with saline. At this stage the area of operation is fully draped and selective excision is performed. Only devitalized tissues, whether they are skin, fat or muscle, are excised—the old concept of "wound excision" being thus truly made an old concept.

Tourniquet.

If one is to generalize about the use of a tourniquet, it may be said that it has a place in clean uncomplicated injuries. Its use may readily prevent assessment of the viability of tissues and add further damage to avascular areas in the contused type of injury, and it is best avoided in this circumstance.

Operative Classification and Assessment.

As the wound is searched and the preliminary excision of tissues is progressing, opportunity is given for detailed assessment of the trauma.

Classification into one of two broad categories is immediately apparent: (i) a clean wound, (ii) a contused, ragged wound. The loss and state of the tissues, their viability and the degree of contamination are revealed. Those suspicions based on clinical test are here proven or denied, and hitherto unsuspected destruction of deep structures becomes apparent.

CLEAN WOUNDS.

A common finger injury is the tangential slice injury. The advent of modern hydraulic presses and the high-speed cutters is commonly the reason for this type of injury. They are clean, purely soft tissue injuries, mostly involving the pulp or nail region. They present a flat, regular surface, which invites a free graft.

Both full-thickness and split-thickness grafts are applicable. In my experience a moderately thick split-thickness graft is durable and has a high "take" rate. It is therefore advised.

Primary closure of existing skin may be preferable in major losses of this type, but necessitates the excision of bone and loss of distance.

Traumatic Amputation.

If the terminal injury to the finger involves section of bone, primary closure with loss of distance is the most commonly applied procedure. The alternative is the application of an immediate pedicle graft, for no free skin will take over exposed bone. This somewhat technical and time-consuming procedure is reserved for members of prime importance—namely, the thumb and index finger.

Incised Wounds with Tendon or Nerve Injury.

As a general rule, primary tendon repair is practised in clean wounds; certainly in extensor tendon injury. It also applies in flexor tendon injuries in certain situations. However, within the fibro-osseous tunnels there is seldom place for either primary or secondary suture, and an elective grafting operation is indicated.

Nerve injury in all but a few cases is treated at a secondary procedure. The assurance of absolute primary healing determines that primary suture of a nerve can be practised in only the cleanest incised wound.

CONTUSED, RAGGED WOUNDS.

Crushed Finger.

The two methods practised in the treatment of crushed finger are similar to those employed in clean wounds. Most commonly elective amputation with loss of distance and the formation of a good stump is to be preferred. "Repulping" is again reserved for injuries involving the most important digits.

Deep Wounds of the Fingers or Hand.

In deep wounds of the fingers or hand a decision has to be made in regard to closure. At least partial closure is possible, and closure by skin graft may be used alone or combined with atension suture.

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Deep structures are often involved, and the principles already enumerated apply even more so in these cases. Healing by first intention is less likely to obtain, and deep repair may well be jeopardized.

Avulsion Injury.

Experience is necessary in making the many decisions required in the surgical treatment of avulsion injury. Obviously avascular tissues will, of course, be removed; but difficulties arise in deciding about the less apparent degrees of avascularity in tissue. To the hand, skin is valuable, and it is a sound rule always to conserve first and remove later. This allows nature to determine the line of section, not the surgeon's knife.

Closure is best achieved by atension suture, but only in certain areas will this be possible. True skin deficiency may well necessitate free or even immediate pedicle grafting.

Conclusion.

The principles which direct the primary management of hand injury have been enumerated, but no attempt has been made to consider the elective surgery of the secondary management in this presentation.

Acknowledgement.

It is desired to record that the subject matter of this paper was similarly presented at the Annual General Revision Course, 1955, of the Post-Graduate Committee in Medicine in the University of Sydney.

CONTROL OF STAPHYLOCOCCAL INFECTION OF THE NEWBORN BY THE TREATMENT OF NASAL CARRIERS IN THE STAFF

By PHYLLIS M. ROUNTREE, MARY HESELTINE, JUDITH RHEUBEN and R. P. SHEARMAN,

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DURING the past ten years there has been an increasing incidence among the newborn in hospital nurseries of infection with *Staphylococcus aureus*, particularly in Canada and the United Kingdom. In Australia, the problem of the prevention of such infections has been raised in acute form by the prevalence of an "epidemic" strain that has been responsible for a large proportion of recent outbreaks of neonatal infection (Rountree and Freeman, 1955).

Investigation of a number of these Australian outbreaks revealed the presence among the nursing and medical staff of nasal carriers of the "epidemic" strain; often these carriers had a history of recurrent furunculosis. In most hospitals only a few carriers were harbouring the strain in question. However, in spite of rigid precautions in the nurseries, infections of the newborn had continued while these carriers were in contact with the babies.

In addition to these infections with "epidemic" strains, there exist, in all maternity hospitals, sporadic infections which can be kept to a minimum by careful nursing techniques, but which it seems impossible to eliminate completely in large hospitals. There is substantial evidence to implicate the nasal carriers in the nursing staff as sources also of these infections (Rountree and Barbour, 1950; Barber, Wilson, Rippon and Williams, 1953).

The problem of the control of both sporadic and epidemic infections may therefore be reduced in its simplest terms to the problem of eliminating the nasal carriers in the staff.

The application to the nose of ointments containing antibacterial substances has been suggested for this purpose. One of the advantages of such methods is that persons being treated can stay on duty during the treatment. Gould and Allan (1954) reported that, in a general hospital in Edinburgh, the incidence of staphylococcal cross-infection of surgical wounds, of varicose ulcers and of the skin and eyes of children was reduced to a low level following the treatment of nasal carriers in the staff. Local application of an antibiotic cream containing 1% oxytetracycline eliminated the staphylococci from the noses of 31 out of 34 carriers.

For a number of reasons the tetracyclines may not be ideal substances for the treatment of nasal carriers. In many hospitals there is a high incidence of infection with staphylococci resistant to the tetracyclines, and this is associated with a large number of carriers of these resistant strains. Furthermore, the administration of these antibiotics can lead to the development of resistance in previously sensitive strains, and it would seem undesirable to use them more often than is strictly necessary or for purposes other than therapy of clinical infections.

Accordingly, at the suggestion of Dr. E. F. Thomson, we have investigated the effectiveness of an ointment containing bacitracin and neomycin, two substances never used for parenteral or oral therapy. The presence of two antibiotics in a single preparation has the additional advantage that mutants resistant to both have a very small probability of occurrence.

The occasion for this trial arose when it was observed that there was a rising incidence of staphylococcal infection of the newborn in King George V Hospital for Mothers and Babies. On being advised of the increase in staphylococcal infection, the honorary medical staff appointed, from its senior members, a committee to consider the problem. This committee approved the project of the trial.

Incidence of Infection of the Newborn.

The incidence of *Staph. aureus* infections of the newborn in the nurseries of the hospital for the years 1952 to 1954 and for the first four months of 1955 is shown in

TABLE I.

Incidence of Staphylococcal Infection of the Newborn at King George V Hospital, January, 1952, to April, 1955.

Period.	Number of Live Births.	Number of Infections.			Infection Rate. (*Per Centum.*)
		Eyes.	Other Lesions.	Total.	
1952	3947	41	25	66	1·67
1953	4106	85	41	126	3·07
1954	4254	94	144	238	5·59
1955—					
January ..	328	0	7	16	4·86
February ..	375	11	25	36	9·60
March	372	4	24	28	7·70
April	355	14	19	33	9·06

Table I. The incidence of infection was obtained from the laboratory records, and the figures therefore represent bacteriologically proven cases.

There is a strict rule that material for culture must be taken from all babies showing clinical evidence of conjunctivitis or skin sepsis, and it is unlikely that any serious cases of infection were missed.

The monthly figures indicate a low incidence throughout 1952 and in the first seven months of 1953. The incidence started to rise in August, 1953. The infection rate in 1954 was 5·59%.

Early in February, 1955, there was a pronounced increase in the numbers of babies suffering from skin lesions. Some of these infections were of a pemphigoid nature, the occurrence of large blisters being their main feature. Phage typing showed that the infecting strains in all these blisters were identical, being phage type 42E. Strains from pustules in a number of other babies belonged to a variety of types.

Phage typing was carried out on 87 strains isolated between December, 1954, and April, 1955, and the incidence

TABLE II.

Distribution of Phage Types Isolated from Lesions of the Newborn and from Noses of the Hospital Staff, King George V Hospital, 1955.

Phage Group.	Babies: Lesions.			Staff: Noses.		
	Strains in Group.	Patterns in Group.		Strains in Group.	Patterns in Group.	
		Pattern.	Number.		Pattern.	Number.
I	11 (12·6%)	52A/79 80 2 others	4 5 2	21 (19·8%)	52A/79 80 8 others	4 5 12
II	3	3 patterns		6	5 patterns	
III	53 (60·9%)	7/42D/42E/53/73 7/42E/47/53/54/75/77 7/47D 42E 47 53 53/73/75 11 others	6 3 2 22 3 3 3 13	50 (47·1%)	7/42D/42E/53/73 7/47D 42E 47 47C/47D 53 20 others	3 6 6 4 4 5 22
IV	1			1		
N.C.	8	29/31B/42D/53 5 others	2 6	15	29/31B/42D/53 11 others	2 13
NT	11			13		
Total	87	31 patterns		106	53 patterns	

of various phage patterns is given in Table II. It will be noted that there were five infections with type 80, the "epidemic" strain isolated elsewhere in Australia. Three of these infections occurred early in December in the general nurseries of the hospital; the other two were in twins admitted to the segregation nursery and born elsewhere. There was no further spread of this strain in the hospital.

Early in February the wearing of masks by all persons handling the babies was instituted, this practice hitherto having been confined to the staff of the premature nursery. However, the skin lesions continued to occur, and there was also a high incidence of conjunctivitis, the average infection rate from February to April being 8·8%.

Survey of Nasal Carriers in the Staff.

In April, it was decided that an attempt should be made to reduce the incidence of infection by treating all nasal carriers of *Staph. aureus* in the staff with "Neotracin" ointment.

Accordingly, a survey of the nasal carrier rates was carried out, swabs being examined from all members of the obstetric staff, including doctors, nurses and physiotherapists, and also from the secretarial and domestic staff. The carrier rates found are given in Table III.

The rates for the lay staff are set out separately, since these people had not only a low carrier rate but also a low incidence of penicillin-resistant staphylococci. This was particularly interesting in view of the fact that many of this group were domestic workers whose duties included the cleaning of the wards and nurseries. The low incidence of penicillin-resistant staphylococci in these carriers suggests that the dust of the wards was not heavily contaminated with these organisms.

On the other hand, the incidence of nasal carriers was higher in the medical and nursing staff, and 73 out of 101 strains isolated were penicillin-resistant. There was no significant difference between the rates in the medical staff and in the nursing staff. Included for comparison in Table III are the carrier rates found in the staff of the Royal Prince Alfred Hospital in December, 1954 (Rountree and Freeman, unpublished observations). These rates are higher than those found in the King George V Hospital.

All the strains isolated were phage typed. Those from the medical and nursing staff comprised many patterns, and in Table II their frequency distributions may be compared with those found in the infected babies. With few exceptions, all the strains isolated from babies were found in the staff. It will be noted that there were five carriers of the type 80 strain. One of these strains was isolated from a nursing assistant who was suffering from a stye and had been taken off duty. One was in a nursing assistant who had just joined the staff; this person was found to be suffering from impetigo and left the hospital the next day. Two carriers were members of the medical staff who had recently suffered from furunculosis. The fifth carrier was a member of the lay staff and carried a penicillin-sensitive strain.

The typing results confirmed those of previous investigations, which pointed to the staff as potential sources of infection for the babies.

TABLE III.

Nasal Carrier Rates of Staphylococcus Aureus in the Staff of King George V Hospital, April, 1955, and in the Staff of Royal Prince Alfred Hospital, December, 1954.

Category.	Number of Subjects Who had Swabs Examined.	Carriers of *Staphylococcus aureus*.	
		Total Number.	Penicillin-Resistant.
King George V Hospital—			
Lay staff	83	24 (29·0%)	3 (12·5%)
Medical and nursing staff	237	101 (42·6%)	73 (72·3%)
Royal Prince Alfred Hospital—			
Medical and nursing staff	250	144 (57·6%)	114 (79·2%)

Treatment of Carriers with "Neotracin" Ointment.

Method of Treatment.

The ointment used contained 3·5 milligrammes of neomycin and 500 units of bacitracin per gramme of a bland base, and was dispensed in small tubes, each containing seven grammes of ointment.

The nasal carriers in the nursing staff were chosen for treatment. The lay staff were not included in the trial, as the phage typing results indicated that they were an unlikely source of infection. Although carriers among the medical staff used the ointment, it proved difficult to arrange for their follow-up examination, and the results

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of their treatment have therefore been excluded from this report.

The purpose of the trial was explained to the nursing staff, and each carrier was then given a tube of the ointment, which she was asked to apply to the inside of the nose three times a day for a week.

Swabs were examined a week after the course of treatment ended and further swabs a month later.

While it was realized that a proportion of the nurses were unlikely to be conscientious in their use of the ointment, this method of arranging the treatment without supervision was adopted as a practicable one, and it was hoped that the results would be an index of what might be anticipated if the method should be adopted generally and on a large scale.

Results of Treatment.

Seventy-four nurses commenced the treatment, but at the end of the first fortnight, when the second nasal swabs were taken, ten were not available; some had completed their training and left the hospital, while others were away on leave or were ill. The results obtained are shown in Table IV. The swabs from 28 (43·7%) of the previous

Table IV.

Nasal Carrier Rates in Nurses Following Treatment of Carriers with "Neotracin" Ointment.

Time After Treatment Ended.	Total Number.	Category.	Number.	Percentage.
1 week.	64	1. Non-carriers	28	43·7
		2. Carriers:		
		(*a*) Same strain .. 22	36	56·3
		(*b*) Different strain .. 14		
5 weeks.	52	1. Non-carriers:		
		(*a*) At 1 and 5 weeks 13	19	35·8
		(*b*) At 5 weeks only .. 6		
		2. Carriers:		
		(*a*) Same strain on 3 occasions 14	33	64·2
		(*b*) Same strain at 1 and 5 weeks .. 8		
		(*c*) Same strain at 0 and 5 weeks .. 6		
		(*d*) Week 1, negative, week 5, new strain .. 1		
		(*e*) Weeks 0 and 1, same strain, week 5, new strain .. 2		
		(*f*) Weeks 0, 1 and 5, different strains .. 2		

carriers yielded negative findings. Of those carrying *Staph. aureus*, 22 (34·3%) were still harbouring their original strain, while in the remainder (22%) a different strain had replaced the previous one. During inspection of the plates, it was noted that in many cases the numbers of colonies of *Staph. aureus* on the "positive" plates were much reduced in comparison with those that had been present on the plates inoculated from the original swabs.

Previous experience (Rountree and Barbour, 1951) had shown that, in the absence of any therapy, approximately 15% of carriers would be expected to lose their strains over a period of four weeks, and that it was rare for a new strain to supplant one already present. It was concluded, therefore, that the "Neotracin" therapy had been responsible for clearing the noses of a significant number of carriers, and that those carrying different strains had acquired them during the week between the termination of treatment and the repeat taking of swabs.

All the strains isolated from the repeat swabs were tested for resistance to neomycin and bacitracin. None was resistant to either of the antibiotics.

The results of phage typing of the strains did not indicate that any phage group or particular pattern in a phage group was more difficult to eradicate than any other.

The next swab taken a month later was expected to produce information on the rate of recolonization of the nose after treatment. On this occasion, the number of nurses available for the taking of swabs was reduced to 52. If during the intervening month the nurse had been ill or away on leave, she was excluded from the trial. The results, given in Table IV, show that 35·8% of the nurses were non-carriers; these included six who had been carriers at the second swab taking and who had therefore lost their strain in the absence of treatment. Five nurses had acquired new strains during the month; of these, two had had different strains at each swab taking and can be regarded as occasional carriers.

Of particular interest, however, were six nurses whose swabs gave negative results after treatment, and from whom, on the third occasion, their original strain was isolated. Possible explanations of this finding include reinfection from contaminated articles of clothing, or the persistence of the organisms in portions of the nasal sinuses inaccessible to the antibiotics.

Reasons for Failure of Treatment.

Antibiotic sensitivity tests having shown that failure of the ointment to clear the nose was not due to the development of resistant organisms, other reasons for failure were considered. One obvious explanation was that the ointment

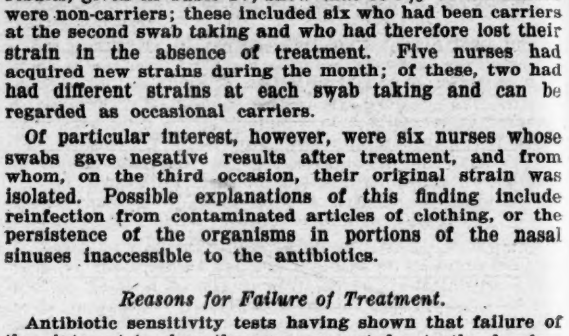

Figure I.

Weekly incidence of neonatal staphylococcal infection in King George V Memorial Hospital from January to July, 1955.

had not, in fact, been used adequately or even at all. Questioning of some nurses indicated that this was true of a number of them.

Ten nurses who had yielded the same strain on three occasions were therefore given a further course of treatment for a week, the ointment being administered with an applicator by one of us. Swabs were taken from them again a week after the treatment ended. Five of the 10 yielded negative results, but from four the original organism was again isolated, while in one a strain different from the original was found.

It was concluded that failure of therapy when applied on a large scale could be due either to the ointment not being used as prescribed or to its ineffectiveness in some carriers. Half the failures were probably due to inadequate application, and if this was taken into account, then the percentage of nurses from whom the treatment removed their original staphylococci became approximately 83.

Effect of Treatment of the Carriers on the Incidence of Neonatal Infection.

As has already been noted, there had been a high incidence of neonatal infection in the weeks prior to the institution of treatment of the carriers. In the week preceding the commencement of the treatment 13 infections occurred. Treatment of the carriers commenced on April 19 and 20, and five infections occurred during the first part of that week, the last one being identified bacteriologically on April 20. No further infections occurred until

one baby was found to be infected on April 30. During the four weeks from April 23 to May 21, only five infections occurred. Thereafter until the end of July the infection rate remained at a low level (Figure I), the average monthly infection rate from May to July being 2·5%.

No further blister-like lesions caused by type 42E occurred. Four nasal carriers of this strain had been identified in the nursing staff and their nasal carriage cured by the "Neotracin" treatment.

During the 14 weeks to the end of July there were 18 cases of skin infection. Seven of these, which occurred in three different nurseries, were due to one particular strain, a penicillin-sensitive strain of type 3A/3B/3C/51/55. Two carriers of this strain had been identified during the nasal survey. The duties of one were confined to one nursery, and furthermore she was away on leave during some of the relevant times. The other carrier was a sister in the labour ward, but her importance was overlooked, as examination of her third swab had given negative results. However, when a further swab from her was examined in July, she was found once more to be a profuse carrier of the strain in question. There is no doubt that her strategic situation in the hospital had provided her with the opportunity to infect these babies. She has since undergone a further course of nasal treatment, and no further infections with this strain have occurred.

Discussion.

The purpose of the trial was twofold. The first purpose was to ascertain whether treatment of nasal carriers with "Neotracin" ointment was an effective means of curing individual carriers, and the second, whether a reduction in the nasal carrier rate would be accompanied by a reduction in the neonatal infection rate.

From the evidence obtained from the first swabs examined after treatment and from the carriers given a repeat course of treatment, it was concluded that "Neotracin" ointment properly applied can be expected to remove their nasal staphylococci from eight or nine out of every 10 persons treated. This percentage of successes compares reasonably well with that obtained by Gould and Allan (1954) following "Terramycin" treatment. In a relatively small percentage of carriers the organisms may be in situations inaccessible to the ointment, and in some carriers there is the possibility of recolonization of the nose with cocci previously deposited on the carrier's clothing, bedclothing or other articles in her immediate personal environment.

With regard to the second object of the trial, we were impressed by the reduction in the incidence of neonatal infection. This occurred abruptly as soon as treatment of the carriers commenced, and has remained at a low level during the succeeding three months; the elimination of the type 42E infections concomitantly with the curing of the nasal carriers of this strain seemed of particular importance.

Sporadic infections still occurred after treatment, and it is unlikely that these can be completely eliminated in a large obstetrics hospital, into which new reservoirs of staphylococci are continually being introduced. Periods of overcrowding, such as occurred in February, 1955, when 375 live babies were delivered during twenty-eight days, will tend to create conditions favourable to the spread of these sporadic infections. During such periods, which are unavoidable under present conditions, the utmost vigilance in the detection of infected babies should be exercised by the staff.

The possibility must be discussed that factors other than the treatment of the carriers were responsible for the fall in the infection rate. It is frequently stated that skin infections are most likely to occur in the hot, humid months of the year, and that they cease with the onset of cooler weather. It is true that our period of reduced incidence corresponded with that of cooler weather. However, the incidence during these months was lower than that during the previous year and, furthermore, the abrupt fall in incidence occurred while the weather was still warm and humid.

The nasal survey and the treatment of carriers undoubtedly made the nursing staff more conscious of the importance of staphylococcal infection, and it is possible that thereafter the babies were handled with greater care.

The actual numbers of babies born in May and June were fewer than in the preceding months; this reduced the overcrowding in the nurseries. Furthermore, steps were taken to discharge a larger number of mothers early in the puerperium. It is likely, therefore, that a lower density of babies played some part in the reduction of the infection rate. However, in July 378 babies were born, and the infection rate remained at the low level of 2·12%.

During the period of high infection rate, it proved impossible to place all infected babies in the segregation nursery. All those with skin lesions were placed in the segregation nursery, but many of those with conjunctivitis had to remain in the main nurseries. So far as possible, they were nursed apart in small rooms. Nevertheless, under these conditions the possibility of spread of infection from baby to baby was always present. Later, when the infections were small in number and only one or two occurred each week throughout the whole hospital, it was easy to arrange for effective segregation of all infected babies.

When all these factors are considered, we feel that we are justified in concluding that the reduction in neonatal infection was correlated with the reduction in the numbers of carriers. The evidence is in favour of the hypothesis that the curing of approximately half the carriers and the reduction in the numbers of staphylococci in the noses of the remainder were the main factors contributing to the lower incidence of neonatal infection. Once the initial reduction in infection had occurred, it would be followed by a reduction in the overall load of staphylococci in the nursery environments.

After the nose has been cleared of its staphylococci, its recolonization by other strains can take place readily. This happened in a number of nurses, and it is likely that with the lapse of time after treatment the carrier rate will return to "normal". Such an increase in the carrier rate occurred in the group of nurses treated by Gould and Allan (1954). It remains to be determined, therefore, how frequently treatment of nasal carriers should be repeated. The most practicable method of deciding this may be to keep a close watch on the neonatal infection rate and to repeat the treatment when it shows signs of rising.

The efficacy of other ointments such as "Neosporin", which contains neomycin, polymyxin B and bacitracin, should be investigated.

Finally, it should be emphasized that, while in this particular investigation we were concerned with the reduction of a high incidence of sporadic neonatal infections on which was superimposed a mild epidemic due to one particular strain, the majority of recent infections in Australia have been due to a different virulent "epidemic" strain. Experience in other hospitals has shown that this strain must be eliminated from the staff before the infections can be controlled. Our present results indicate that the application of antibiotic ointments to the noses of carriers is worthy of further consideration for this purpose.

Summary.

The incidence of neonatal staphylococcal infection in a large obstetrics hospital is described.

In view of an increase in the infection rate early in 1955, a trial was made of the use of "Neotracin" ointment in the noses of carriers among the nursing staff as a means of reducing the incidence of infection.

The use of the ointment resulted in a reduction in the carrier rate in the nursing staff and in a simultaneous reduction in the neonatal infection rate.

This method of control is considered worthy of further investigation as a means of eliminating carriers of "epidemic" strains and of reducing the incidence of sporadic neonatal infection.

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A NEW METHOD FOR PREVENTING GOITRE IN CANBERRA (THE USE OF IODIZED SALT IN BREAD BAKING).

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ENDEMIC GOITRE is a widespread disease due to an inadequate dietary intake of iodine. It can be prevented by giving sufficient iodine.

Several methods for the prevention of goitre have been used in various countries. The most important of these are as follows: (i) the use of iodized table salt; (ii) the use of iodized domestic cooking salt; (iii) the ingestion of medicated tablets or confection; (iv) the provision of iodized water supplies; (v) the use of iodized salt in bread.

Brief Criticism of these Methods.

Iodized Table Salt.

The use of iodized table salt involves the iodization of "free running" salt used on the table. It has been criticized by Osmond and Clements (1948) in Australia; these workers, as a result of a table salt consumption survey, concluded that many young children (who have most need of the iodine) either did not use table salt or used it in insufficient quantities for the method to be of any value. The level of iodization of table salt recommended for various countries varies from one part of potassium iodide to 10,000 parts of salt for the United States of America to one part of potassium iodide to 20,000 parts for Australia.

Iodized Domestic Cooking Salt.

The use of iodized cooking salt has much to recommend it, since all foods prepared in the home will contain iodine when iodized cooking salt has been added. It is the method used in some parts of Switzerland and in New Zealand.

One criticism of the method is that when much food is processed outside the home, as is often the practice nowadays (for example, bread, cakes, tinned foods, biscuits), little home cooking may be done. It is essential that the vehicle for iodine should be a generally used commodity.

Medicated Tablets (or Confection).

The use of medicated tablets has been adopted in parts of Australia (Canberra, Tasmania, Gippsland) and in parts of Switzerland. In Australia the method is carried out as follows. With the consent of the parents, one tablet containing 10 milligrammes of potassium iodide (7000 microgrammes of iodine) is given each week to children aged from one to fourteen years, and two tablets per week are given to expectant and nursing mothers. The tablets are issued free and are distributed through the schools, baby health centres, chemists and medical practitioners.

A great advantage of the method is that an accurately measured dose of iodine is administered. The main defects of the method are that it is not automatic in operation and that it depends on the interest and cooperation of a great number of people. This cooperation has to be continued year after year. Thus it may be difficult to organize an effective distribution.

Iodized Water Supplies.

In various parts of the world iodized water supplies have been used in the past, but this method has now been abandoned everywhere. The method was used extensively in the Netherlands before and during the early part of World War II, but has now been replaced in that country by the use of iodized salt in bread.

The following are two serious disadvantages in the use of iodized water supplies: (*a*) A very small percentage of the water which is iodized is consumed as drinking water. Hence the method is wasteful of iodine, which is a comparatively expensive substance. (*b*) Only those households connected with a municipal water supply benefit, and therefore it is unsuitable for use in rural areas.

Iodized Salt in Bread.

In countries where bread is a staple foodstuff, and particularly where it is factory baked, it would seem to be a satisfactory vehicle for iodine inclusion. In a bread consumption survey which Hipsley (unpublished data) carried out in a goitrous area of Australia in 1949, it was found that even young children eat bread in appreciable amounts. The frequency distribution of the consumption figures was such that all children would receive an adequate, though not excessive, dose of iodine, if the salt used in bread was iodized at the strength of one part of potassium iodide in 10,000 parts of salt.

It was suggested by some people that when potassium iodide was added to dough, iodine might be lost in the baking process. Using a radio-active iodine trace technique, Hipsley (unpublished data) was able to show that there was no loss of added iodine during bread baking.

The History of Goitre Prevention in the Netherlands.

Goitre occurs in the Netherlands mainly in the eastern and central provinces. The incidence appears to have increased in the last fifty years, but the reason for this increase is not clear.

Before World War II the control of goitre in the Netherlands was undertaken by means of iodized water supplies. Two notable towns having iodized supplies were Utrecht and Delft. The method was generally regarded as satisfactory for the towns, except that it was comparatively costly. It was recognized, however, that a great number of the households were not connected with the town water supplies, and thus were receiving no protection by this method. In 1941 supplies of iodine were cut off by the spread of war and the method was discontinued.

In 1943 the iodized bread method was introduced to make the best use of the small supplies of iodine available, since the method required considerably less iodine than iodization of water supplies. Regulations were gazetted requiring that in some municipalities known to be goitrous and indicated by the Government, only bread baked with iodized salt could be transported and sold. In the bakeries the use of salt other than iodized salt was prohibited. The level of iodization fixed was 39 milligrammes of alkaline iodine per kilogram of salt (one part of potassium iodide in 25,000 parts of salt). No limit of storage time was fixed, as it was considered that any small losses of iodine which might occur during storage of the salt were not significant. The daily per-capita consumption of bread (as flour

TABLE I.

Effect on Incidence of Goitre after Eight Years of Iodization of Bread.

Town (Iodization Introduced in 1948).	Before Iodization of Bread.						After Eight Years of Iodization.					
	Boys.			Girls.			Boys.			Girls.		
	Number Examined.	Size.[1]		Number Examined.	Size.[1]		Number Examined.	Size.[1]		Number Examined.	Size.[1]	
		1	2		1	2		1	2		1	2
Gorinchem (children 6 to 13 years) ..	260	111	7	257	114	12	63	11	0	68	8	0
Noorwijk (children 6 to 12 years) ..	640	109	39	619	214	82	No data			No data		
Noordwijkerhout (children 6 to 13 years)	544	128	24	541	156	49	142	16	0	151	13	0

[1] In estimating goitre size, the classification of Percy Stocks is used. Size 0: thyroid not palpable, or only the isthmus palpable as in thin strap. Size 1: lobes palpable, but not visibly enlarged; or isthmus palpable as thick as a lead pencil. Size 2: thyroid visibly enlarged (unmistakably) when viewed from the side. Size 3: gross enlargement of thyroid.

equivalent) in the Netherlands is approximately 250 grammes. In the baking of bread, salt is added to flour at the rate of one kilogram of salt to 60 kilograms of flour. This level of iodization of salt, therefore, was designed to give a daily per-capita intake of 100 microgrammes of iodine.

Dr. F. Pasma, Gerondheids Organization, T.N.A., has kindly supplied me with results showing the effect of iodized bread since 1945 in three municipalities in south Holland, where goitre is endemic (Table I).

It would appear from the foregoing figures that iodized bread has had an appreciable effect on the incidence of goitre.

Goitre Prevention in Canberra.

Since 1947 it has been the practice in Canberra to endeavour to prevent the occurrence of goitre by issuing free to school children and to expectant and nursing mothers, tablets containing 10 milligrammes of potassium iodide.

Palpation of the thyroid gland of school children over a number of years has produced information which indicates that the method has been moderately effective in controlling goitre. However, the scheme depended for its success on a close degree of cooperation by the health authority, doctors, chemists, school teachers, mothercraft sisters and the individual parents and children. It became apparent that if a more automatic but equally effective scheme could be devised it would be advantageous.

Details concerning a suggestion that iodized salt should be used in the baking of bread in areas of endemic goitre were discussed by the National Health and Medical Research Council at its thirty-fifth session held in May, 1953. The Council carried the following resolution with regard to goitre prophylaxis:

> The Council recommends to the States that bakers of bread for sale in specified goitrous areas be permitted to use iodised salt (1 part of alkaline iodide in 10,000 parts of salt) in the baking of such bread.

As a result of this recommendation, all bakers of bread intended for sale in Canberra now use a special iodized salt for bread-baking purposes. This special salt, which is manufactured by the Cheetham Salt Company of Geelong, Victoria, is of flossy fine grade. It is sold through the Government Store, Department of Works, Canberra, and is made available to bakers at the same cost as ordinary non-iodized salt. The balance of the slightly extra cost of the iodized salt is paid from the Australian Goitre Prevention Fund, established in 1947 by the Commonwealth Government, to pay for the free distribution of iodized tablets to the various States where endemic goitre is prevalent.

Summary.

Different schemes for adding iodine to the diet in areas of endemic goitre are discussed.

Attention is drawn to the use of iodized salt in bread, which has been an effective method for the control of goitre in the Netherlands since 1943. The method has recently been introduced to control goitre in Canberra, and it now replaces the distribution of iodine-medicated tablets to school children and to expectant and nursing mothers.

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THE DIFFERENTIAL LEUCOCYTE COUNT: OBSERVATIONS ON THE ERROR DUE TO METHOD OF SPREADING.

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IT is not the purpose of this paper to discuss the significance of the differential leucocyte count. The very fact that, despite its tediousness, it is always included in a routine complete blood examination is sufficient indication of the place it occupies in clinical medicine at present.

The significance of an error present in the measurement of any quantity must be judged in relation to the minimum extent of change in that quantity deemed to be significant. For instance, if it is the view that only changes of the differential neutrophile percentage greater than ten units are of note, then a factor producing a possible error of only one unit is hardly worthy of consideration. On the other hand, a change of ten units in such a measurement cannot be considered to be significant if there is known to exist a factor producing a possible error of about that number of units. The elucidation of any possible error in the differential count is worth while if such an error is not very much smaller than the minimum variation in the count to which clinical significance is attached. Also, if such an error can be eliminated, the path is clear for the collection of new data on the subject. As a result of this, the importance of variations previously taken to be too small to matter may become appreciated.

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Two errors in the differential leucocyte count have received some attention in the past: the statistical error and the error introduced by the uneven distribution of leucocytes over a smear. The statistical error has been elucidated by a number of people. It suffices to say of this error that when three hundred cells are counted its contribution to the total error in the differential lymphocyte or neutrophile cell count is quite small.

This paper is concerned with the error in the count introduced by the uneven distribution of leucocytes over a smear. The fact that leucocytes do not distribute themselves uniformly in an ordinary blood smear has long been recognized. The tendency for leucocytes to be more abundant at the edges of the smear than in other parts is very easy to recognize. It is not so well recognized that there is a differentiation amongst the leucocytes in this respect. Thus lymphocytes show less of a tendency to congregate at the edges than do the neutrophile cells. This differentiation has been observed and some considerable data about this subject have been collected. The most important contribution has been made by MacGregor, Richards and Loh (1940) and apparently no material advances have been published since that time.

They investigated very fully the variations in the differential count according to the method of traversing the smear. As the present paper will endeavour to continue investigation from the point where MacGregor *et alii* left it, it will be necessary to summarize the main conclusions reached by them.

They made three differential counts of each smear by traversing each one in three different ways. For the straight count the smear is traversed along its edge. For the cross-sectional count the smear is traversed backwards and forwards from one edge to the other in a direction at right angles to that in which the smear was spread. For the battlement count, the smear is traversed partly along the edge and partly inwards to the depth of a few fields.

In 23 smears they made these three differential counts. Also they counted every leucocyte on the smear, including the tail. By counting those in the tail separately they could express this as a tail count. From a consideration of every leucocyte on the smear they arrived at a total count.

The differentiation between the leucocytes manifested itself most markedly in the difference between the lymphocyte percentage of the cross-sectional count and that of the straight count for the same smear. On an average, the ratio of the former to the latter was about two. But variations of this ratio from 1·4 to 3·5 were met with.

The lymphocyte percentage of the total count lay between that of the cross-sectional count and the straight count, though nearer to the latter than the former. The average neutrophile percentage of the straight count was about 15 units higher than that of the cross-sectional count. The average neutrophile percentage of the total count lay between the two, though it was nearer to that of the straight count. The monocyte percentage of the straight count was somewhat higher than that of the cross-sectional count, with that of the total count lying between. There was very little statistical significance in the differences in the eosinophile percentage of the various counts.

It was estimated that in the average smear about 60% to 80% of all the leucocytes were to be found in the tail and the average percentages in the tail count agreed quite closely with the average percentages in the straight count for the four types of leucocytes.

An investigation of the variation of the density of the various leucocytes with varying distances from the edge of the smear revealed that all leucocytes show some increase in density at the edge. This increase is restricted to that part of the smear which is within two millimetres of the edge. Furthermore, the relative increase in density at the edge is much greater in the case of the neutrophile cells than in the case of the lymphocytes. Whereas the density of the lymphocytes at the edge is about double that of the centre, the density of the neutrophile cells at the edge is about four times that of the centre. The increases in density shown by the eosinophile cells and monocytes in this respect are apparently greater than that shown by the lymphocytes, but are less than that shown by the neutrophile cells.

MacGregor, Richards and Loh have regarded the edge of the smear and the tail of the smear as a functional unity. Whenever there is an increase in density of a certain type of leucocyte at the edge of the smear there will also be a similar increase in density of that particular leucocyte in the tail. The discrepancies in the percentages obtained by the various methods of counting may be explained therefore in terms of the different tendencies shown by the several types of leucocytes to be scattered more densely both at the edge and in the tail.

On the basis of the average relationship between the various counts, the above-mentioned investigators made conversion graphs whereby the percentage of any particular type of leucocyte found by one method of counting can be used to determine the percentage that would be found by using any other method of counting. This would provide a basis for the comparison of counts done by one method with counts done by any of the other methods.

This method of approach relies upon the supposition that the tendencies of the several types of leucocytes to congregate at the edge and in the tail remain constant from smear to smear. However, it is patent that these tendencies do not remain constant. This is demonstrated by the data supplied by MacGregor, Richards and Loh themselves. Whereas the average lymphocyte percentage in the cross-sectional count for 72 smears was about double that of the average lymphocyte percentage in the straight count for the same smears, for individual smears the ratio varied from 1·4 to 3·5. Moreover, it is apparent to any careful observer that smears differ very considerably from one to the other with respect to the tendency of leucocytes to congregate at the edge.

The work about to be described followed an attempt by the author to find the reason for this lack of constancy among smears. To begin with, many different methods of making the blood smears were tried. Smears were made at different temperatures, with spreaders of different widths, after allowing the drop to stand for some time before spreading, with larger and smaller drops of blood and by spreading at different speeds. It fairly soon became obvious that the most important factor is the rate at which the spreader is moved across the slide, and the data presented will therefore be restricted to what was found by varying the rate of spread.

Method.

The smears were made on slides of standard size three inches by one inch. The slides had been passed through alcohol and then ether, and finally polished with a silk cloth.

There is no doubt that it is easier to make an even smear with a thin spreader than with a thick one. The advantage of the thin spreader probably lies in its flexibility. This allows it to make even contact with the surface of the slide even though this surface is not perfectly plane. Naturally, a spreader that is too thin will break too easily, and a compromise is reached by using coverslips of gauge two or three. The coverslips were three-quarters of an inch wide and the edges of the smear therefore lay well within the slide.

The rate of spreading is probably the most important factor determining the thickness of the smear. Smears which are spread slowly are inevitably thin. Spreading was done by hand and, for the slowly spread smears, the movement was made as slowly as it was possible to do so without its becoming uneven. The time taken for such a spreading would be between one and two seconds. The smears so formed were about two inches long and never more than one cell thick, and appeared entirely suitable for a differential count in any part.

The smears spread rapidly were inevitably thick. In most places they were too thick for use in differential

counting. To obtain a smear about two inches long it is necessary to take a much larger drop of blood than one needs for a slowly spread smear. Rapidly spread smears are always thicker near the beginning than near the tail, and it is possible to find a part near the tail that is suitable for a cross-sectional count. As these smears are thinner at the edges it is quite easy to make a straight count on them. It is impossible to give an accurate estimate of the time taken to spread such smears. It can be said only that they were spread as fast as possible.

Fast smears and slow smears were made from the blood of one individual from the same bleeding point and with as little delay as possible. The smears were treated with Leishman stain and the counts were made by using a ×10 eyepiece and a $^1/_{12}$ oil immersion objective with an overall magnification of 900.

In the case of the straight counts made on the rapidly spread smears a minimum of 200 cells was counted; but in all other cases the minimum number was 300.

As it has been shown that there is no significant difference between the cross-sectional count made at one end of the smear from that made at the other, no special attention was paid to the exact part in which this count was made. However, in all cases the part of the smear near to the tail was traversed in making this count.

Results.

The percentages of lymphocytes, neutrophile cells, eosinophile cells and monocytes found in the straight counts and cross-sectional counts both for the rapidly spread and slowly spread smears of twelve individuals are to be found in Table I.

It is quite obvious that whereas there are large differences between the percentages found by the two methods of counting on the slowly spread smears, there is little difference between these percentages on the smears which are spread rapidly.

This point may be illustrated by considering the ratio of the lymphocyte percentage found by the cross-sectional count to that found by the straight count on the same smear. For the smears which are spread slowly the extreme values of this ratio are in the range of 1·53 and 2·40, and the average of all the values is 1·94. For the smears spread rapidly the extreme values of this ratio are 0·82 and 1·14, and the average of all the values is 1·01.

This same point may be further demonstrated by considering the average of the monocyte percentages as found by the various methods. For the rapidly spread smears the average of the monocyte percentages of the cross-sectional counts is 6·3 and that for the straight counts is 6·8. For the slowly spread smears the average of the monocyte percentages of the cross-sectional count is 4·2 and that for the straight counts is 9·3.

Since there is so little difference between the two counts made on the rapidly spread smear, we have taken the average of these values and will refer to this simply as the count on the rapidly spread smear.

The cross-sectional count on the slowly spread smear differs from the count on the rapidly spread smear in the following respects: (i) its lymphocyte percentage tends to be higher; (ii) its neutrophile percentage tends to be lower; (iii) its monocyte percentage tends to be lower.

The ratio of the lymphocyte percentage of the cross-sectional count on the slowly spread smear to that of the count on the rapidly spread smear has the extreme values of 1·35 and 1·91, and the average of all the values is 1·59.

The straight count on the slowly spread smear varies from the count on the rapidly spread smear in the following respects: (i) its lymphocyte percentage tends to be lower; (ii) its neutrophile percentage tends to be higher; (iii) its monocyte percentage tends to be higher.

The ratio of the lymphocyte percentage of the rapidly spread smear to that of the straight count on the slowly spread smear has the extreme values of 0·98 and 1·68, and the average of the values is 1·25. It is apparent, therefore,

TABLE I.

Results Demonstrating Comparison between Cross-sectional Counts, C, and Straight Counts, S, Carried Out Both on a Slowly Spread Smear and on a Rapidly Spread Smear from Each of 12 Individuals.

Blood Source.		Slowly Spread Smear.				Rapidly Spread Smear.			
		L.[1]	N.[2]	E.[3]	M.[4]	L.	N.	E.	M.
C.T.	C ..	53·2	43·9	0·6	1·3	37·6	53·9	2·2	6·2
	S ..	22·2	65·8	3·8	7·6	36·8	50·9	3·7	8·0
P.C.	C ..	58·4	37·4	0·7	3·0	32·7	57·3	1·7	7·0
	S ..	27·5	59·0	2·5	11·0	32·5	58·5	0·5	8·0
G.P.	C ..	46·0	40·0	6·5	6·0	32·3	53·7	7·0	6·7
	S ..	25·5	53·5	7·0	13·5	36·0	49·0	3·5	11·0
W.V.	C ..	43·6	48·4	1·2	5·6	27·7	63·3	0·7	7·3
	S ..	20·9	66·1	2·4	10·3	26·0	63·0	2·0	8·0
W.S.	C ..	74·8	19·6	1·6	3·2	41·7	52·3	0·7	4·3
	S ..	38·0	51·7	1·0	8·3	36·5	54·5	3·5	5·0
N.H.	C ..	46·3	49·0	0·7	4·3	28·7	62·0	0·7	8·0
	S ..	22·3	64·7	1·3	11·7	27·9	62·1	2·0	7·9
G.B.	C ..	47·7	44·3	2·7	5·3	34·7	54·0	2·3	8·7
	S ..	24·3	62·3	2·3	10·7	34·5	54·5	2·0	8·5
A.C.	C ..	37·3	47·3	9·7	4·0	27·7	51·3	14·0	4·3
	S ..	24·4	50·4	19·2	5·2	26·0	52·0	16·7	4·7
S.S.	C ..	33·3	59·7	1·0	6·0	24·3	67·3	1·0	7·3
	S ..	19·0	71·0	0·7	9·3	23·0	69·7	1·0	5·7
N.S.	C ..	37·0	52·7	5·0	3·7	25·3	60·0	9·7	3·3
	S ..	17·3	67·0	6·0	8·3	25·3	61·5	8·0	4·0
B.G.	C ..	58·3	38·3	0·3	3·0	31·7	61·0	1·3	5·7
	S ..	30·9	60·4	0·4	7·8	31·5	61·0	2·0	5·5
J.W.	C ..	40·3	51·3	4·0	4·3	23·0	66·5	3·0	7·0
	S ..	26·0	61·0	3·3	7·3	28·2	61·7	3·8	5·3

[1] Lymphocytes *per centum.*
[2] Neutrophile cells *per centum.*
[3] Eosinophile cells *per centum.*
[4] Monocytes *per centum.*

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that in this respect the straight count of the slowly spread smear lies closer to the count on the rapidly spread smear than does the cross-sectional count.

The monocyte percentage of the straight count on the slowly spread smear tends to be considerably higher than the monocyte percentage of the rapidly spread smear, whereas the monocyte percentage of the cross-sectional count on the slowly spread smear tends to be considerably lower than the monocyte percentage of the rapidly spread smear.

A big difference between the rapidly spread and the slowly spread smears is readily apparent under inspection with the low power of the microscope. The slowly spread smears uniformly contain a marked concentration of leucocytes near their edges. This phenomenon is absent in the case of the rapidly spread smears. In order to illustrate this difference in a quantitative fashion, a separate count was made of the cells in the edge fields in the smears from one individual. In this case, for the cross-sectional count of the slowly spread smear there was a total of 314 cells, of which 216 lay in the edge fields. For the cross-sectional count of the rapidly spread smear, for the same individual, there was a total of 500 cells, of which only nine lay in the edge fields.

In the slowly spread smears it is not uncommon to come across groups of up to 20 leucocytes lying along the edge. These are never met with in the rapidly spread smear.

The other notable difference between the two types of smears lies in the concentration of leucocytes relative to that of the erythrocytes in the body of the smear. The concentration of the erythrocytes in the parts traversed whilst the cross-sectional count was being made was not so very much greater in the case of the rapidly spread smears than that in the slowly spread smears; yet there was a tremendous difference in the numbers of leucocytes found in one traverse across the smear.

In one slowly spread smear the average number of cells seen during one traverse across the smear was about three and in another it was 20. These were the extreme cases, and for the others the numbers were usually not far from 10. In one rapidly spread smear the average number of white cells seen during one traverse was 100 and in another it was 25. These were the extreme cases, and for the others the numbers were nearer to 60.

Discussion.

Whilst it is not an integral part of the argument of this paper, it is important to realize that there is probably not much difference between our slowly spread smears and the ordinary smears submitted for routine examination in general clinical practice. Furthermore, there is certainly not much difference between these smears of ours and those used by MacGregor, Richards and Loh. To support this claim we can mention the ratio of the lymphocyte percentage of the cross-sectional count to that of the straight count. In our slowly spread smears the average of these ratios was 1·9, and in the smears used by MacGregor, Richards and Loh the average was almost the same. If the general arguments of this paper are accepted, then this can be taken as evidence that from the point of view of leucocyte distribution the two groups of smears are comparable.

For the explanation of the observations outlined in the table we can regard any smear as being divided into two functional units: (i) the body, (ii) the edge and the tail.

Each type of leucocyte has a tendency to migrate during the spreading so as to be deposited either in the edge or in the tail. This tendency is much greater in the case of the neutrophile cells, the monocytes and the eosinophile cells than it is in the case of the lymphocytes. Also it can become manifest only when the smear is spread slowly, and becomes more manifest as the smear is spread more slowly.

These hypotheses will explain all the major differences in respect to leucocyte distribution that we have found to exist between the rapidly spread and the slowly spread smear. It hardly needs to be added that if this reasoning is accepted, it becomes a very powerful argument for the use of a rapidly spread smear in the making of a differential count. For this represents the nearest approach, short of counting all the leucocytes in a smear, that it has been so far possible to make to the true differential count.

Apart from being nearer to the true count, it has in its favour, owing to the much greater concentration of leucocytes, that it is much less tedious to make than a cross-sectional count on a slowly spread smear. The count on the rapidly spread smear can be made in about one-third of the time it takes to make the latter count. It should be pointed out, however, that rapidly spread smears are usually too thick to be used to study the morphology of leucocytes. This should always be done on a slowly spread smear.

Summary.

Observations have been described indicating that with rapidly spread blood smears the leucocytes are distributed fairly uniformly throughout the smear. This is in contrast to the slowly spread smears in which the leucocytes become concentrated in the edges and tail.

The extent to which this concentration takes place varies according to the type of leucocyte.

It follows that a differential count performed upon a rapidly spread smear will be much closer to the true count than one performed upon a slowly spread smear.

Reference.

MACGREGOR, R. G. S., RICHARDS, W., and LOH, G. L. (1940), "Differential Leucocyte Count", *J. Path. & Bact.*, 51: 337.

Reports of Cases.

PROTHROMBIN ACCELERATOR DEFICIENCY ASSOCIATED WITH TUBERCULOSIS.

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PROTHROMBIN ACCELERATOR is a name given to a plasma globulin which is essential for conversion of prothrombin into thrombin under physiological conditions (Fantl and Nance, 1946*a*, 1946*b*, 1948; Fantl and Everard, 1949). Synonyms in use at the present time are labile factor (Quick, 1947*a*), Ac-globulin (Ware, Guest and Seegers, 1947) and proaccelerin (Owren, 1951). A hæmorrhagic tendency due to deficiency of this compound was found by Owren (1947). Since that time a number of reports have indicated that prothrombin accelerator deficiency can occur as a congenital and familial defect (Quick, 1947*b*; Frank *et alii*, 1950; de Vries *et alii*, 1951; Stohlmann *et alii*, 1951; Alexander and Goldstein, 1952; Brink and Kingsley, 1952; Owren, 1953; Field and Ware, 1954), or it can be acquired during experimentally induced hepatic damage (Sykes *et alii*, 1948) or in hepatic disease (Alexander and Goldstein, 1950; Hartman and Langer, 1950), in scarlet fever (Koller *et alii*, 1950), in leuchæmia (Alexander *et alii*, 1949), and in carcinoma of the prostate (Cosgriff and Leifer, 1952).

We wish to report an unexpected association of prothrombin accelerator deficiency and tuberculosis, and some peculiarities in this coagulation defect.

Clinical Record.

Mrs. K.L., aged sixty-six years, was admitted to the Alfred Hospital on September 28, 1953, suffering from acute blood loss. She had been in good health until nine months previously, when she had an attack of hæmaturia lasting for six days. A month later she began to suffer from recurring epistaxes and excessive bruising following trivial injuries. Loss of weight and well-being then followed an attack of "influenza". Two months before her

[1] Part of the expenses of this investigation were defrayed by a grant from the National Health and Medical Research Council, Commonwealth of Australia.

[2] McComas Research Fellow.

admission to hospital she was taken to another hospital on account of a severe epistaxis, and bilateral pleural effusions were found.

After her discharge from that hospital a mass appeared in the right buttock. This was excised, and two days later the wound began to bleed freely. A further severe epistaxis led to her admission to the Alfred Hospital. Her complaints were weakness and dyspnœa even at rest, and a slight cough of several weeks' duration, with the occasional appearance of small blood clots in the sputum.

There was no previous history of hæmorrhage. She had had complete dental extraction at the age of twenty-five years without serious bleeding. Her menstrual loss had never been excessive, and no abnormal bleeding had followed three confinements.

Although the patient denied a family history of bleeding, subsequent inquiry revealed that a niece, M.T., had been a bleeder. A pedigree which included 96 members was obtained. Part of the pedigree is shown in Figure I.

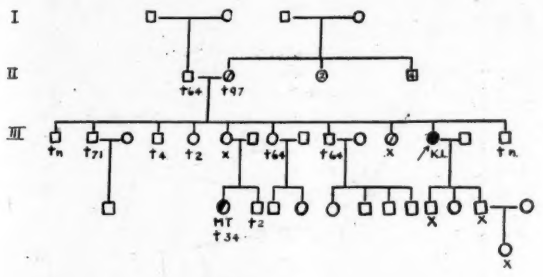

FIGURE I.

Part of the pedigree of K.L. Hæmorrhages were experienced by four members only. No evidence of consanguinity was found. "○", normal on clinical examination and laboratory testing; "◐", slight epistaxis; "◑", severe hæmorrhages; "●", fatal hæmorrhage; "$\overset{\circ}{+2}$", age at death; "n", neonatal.

The niece M.T. (IV 2, in the pedigree) had her first hæmorrhages at the age of eight years. Until she died at the age of thirty-four years in 1939, she had been a chronic invalid as the result of severe epistaxes, and of prolonged bleeding following injuries and tooth extraction. Her relatives cannot remember her menstrual loss being excessive. No details of investigations are available.

The mother (III 6) of M.T. had never experienced excessive bleeding, but is suffering from pulmonary tuberculosis. The only other bleeding known to have occurred in the family is an occasional minor epistaxis suffered by II 2 and by III 12.

Examination of the patient showed the presence of bilateral pleural effusions, finger clubbing of moderate degree and severe pallor. The biopsy wound in the buttock was bulging with blood clot and oozing a little bright blood. There were some bruises on the arms and hands. Apart from weight loss, no other abnormality was found. Chemical and microscopic examination of the urine gave normal findings. The hæmoglobin value was 5·9 grammes *per centum*. A reticulocytosis of 20% and a neutrophilic leucocytosis were found. The coagulation data are given in Table I. X-ray examination of the lung fields indicated bilateral effusion, but the lung fields were otherwise clear. Transfusion with citrated blood brought the hæmoglobin level to normal. On October 15 a direct transfusion with 650 millilitres of blood preceded *paracentesis thoracis*. The fluid obtained was lightly blood-stained and was reported to contain *Mycobacterium tuberculosis*, which was demonstrated by examination of a direct smear, guinea-pig inoculation and culture techniques. Examination of urine, sputum and gastric juice failed to reveal any organisms. Pyelographic examination revealed no abnormality. The results of liver function tests carried out on two occasions were normal.

Treatment with streptomycin (0·5 gramme *per diem*) and "Isoniazid" (0·2 gramme *per diem*) was commenced on October 28. On November 11 further aspiration of the pleural cavities was carried out for the relief of dyspnœa, and frank blood was obtained. Epistaxis commenced on November 14, and uncontrollable gastro-intestinal bleeding occurred. The patient died on November 15, in spite of repeated transfusions of fresh blood.

Post-Mortem Examination.

The pleural cavities contained large amounts of fluid and clotted blood. The lungs were densely adherent to the chest wall over the bases and lateral surfaces. Apart from apical scarring there was no evidence of active parenchymatous tuberculosis of the lungs. The peritoneal surfaces were covered with tiny yellow-grey tubercles. The stomach and intestines contained a large amount of black material resembling altered blood. Histological examination of the peritoneum revealed typical tuberculous lesions. The liver was normal apart from a small amount of hæmosiderin in the parenchymal cells, particularly around the central (hepatic) veins, and a few scattered inflammatory cells in the portal tracts. (The biopsy report on tissue taken from the buttock indicated non-specific chronic inflammatory changes in the fat.)

Pathological Investigations.

The coagulation data are given in Table I.

TABLE I.
Coagulation Data.

Observation.	Patient.	Normal.
Whole blood clotting time in minutes:		
37° C. in glass	17 to 19	9 to 19
37° C. in silicone	105	40 to 110
Skin bleeding time in minutes, 37° C. (Copley and Lalich, 1942)	<2	1·5 to 3
Plasma prothrombin time in seconds (Quick, 1951), seven determinations	30 to 60	10 to 15
Prothrombin assay in units per millilitre of oxalated plasma (Fantl, 1954*a*), five determinations	310 to 340	320 to 600
Serum prothrombin time in seconds	∞, 14·5	30 to ∞
Prothrombin assay in units per millilitre of serum	210 0	0 to 30
Alpha-prothromboplastin per millilitre of blood (Fantl, 1954*b*)	100	80 to 200
Beta-prothromboplastin per millilitre of blood	100	80 to 200
Fibrinogen (milligrammes per 100 millilitres)	360	200 to 400
Fibrinolysis	Absent	—
Thrombin clotting time in seconds	20	17
Plasma recalcification time[1]	690	140 to 270
Thrombocytes per cubic millimetre	340,000	150,000 to 400,000
Clot retraction	Normal	—
Serum protein content (grammes *per centum*)	4·6 to 5·6	7 to 8

[1] The addition of 20% of patient's plasma to normal plasma did not alter the recalcification time of the latter, which indicates the absence of inhibitors in the patient's blood.

From the results given in Table I it is apparent that the prothrombin clotting time of the patient's plasma was considerably prolonged and fluctuated during the period of observation. On the other hand, the actual prothrombin concentration was constant and within the normal range. This suggested that the hæmorrhagic state was due to a plasma defect causing delayed thrombin formation. From the results given in Table II it will be seen that the relatives showed a normal prothrombin time and concentration, and since the rate of thrombin formation was the same as in normal control specimens, which was 1·5 minutes, it is certain that none had a defect of the prothrombin complex. A more detailed study of the anomaly was carried out. Prothrombin clotting times were determined from mixtures containing the patient's oxalated plasma, and normal oxalated plasma freed of prothrombin by treatment with barium sulphate suspension (Ba-plasma). These results are given in Figure II.

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The curves given in Figure II show that the addition of normal Ba-plasma to the patient's plasma shortened the clotting time, and that between 60% and 80% of Ba-plasma was required to correct the deficient prothrombin time. The patient was given an intravenous injection of an emulsion of 50 milligrammes of vitamin K_1 ("Mephyton", Merck). Blood taken twenty-four hours later showed unaltered prothrombin clotting times, indicating that vitamin K_1 had no effect. This is in contrast to our experience in true hypoprothrombinæmias induced by dicoumarol drugs, in which benefit is given by vitamin K preparations. In further investigations various additions to the patient's plasma were made and the prothrombin time of mixtures was determined. The results are given in Table III.

The additional information gained from the results in Table III is that in contrast to normal plasma (Experiment X) the patient's plasma (Experiment IX) and Ba-plasma prepared from it (Experiment VIII) did not correct the deficient prothrombin clotting time of stored plasma.

TABLE II.

Prothrombin Results of Patient and of Her Relatives.

Subject.	Plasma Prothrombin Time in Seconds (Quick).	Prothrombin Assay.	
		Units per Millilitre of Oxalated Plasma.	Time of Maximal Thrombin Formation in Minutes.
1. Patient (III·13) ..	30 to 60	310 to 340	8 to 11
2. Sister (III 6) ..	11	420	1·5
3. Sister (III 12) ..	9·5	600	1·5
4. Son (IV 10) ..	9·5	510	2
5. Son (IV 12) ..	10	510	1·5
6. Niece (V 1) ..	10	528	1·5
Normal controls	9·5 to 11	320 to 600	1·5 to 2

Further, the prothrombin time of patient's plasma could be partly improved by the addition of normal serum (Experiment V); the patient's serum had little, if any, activating effect on normal plasma (Experiment XI). These results made it necessary to investigate the dynamics of the thrombin formation in the patient's plasma. This was carried out by an assay procedure (Fantl, 1954*a*). The results are plotted in Figure III.

The results given in Figure III show that the patient's plasma formed thrombin at a rate slower than normal plasma; but after a delayed reaction time the maximal amount of thrombin was formed. The rate of thrombin formation of the patient's plasma could be increased by the addition of normal Ba-plasma and also by the addition of normal serum. But the yield of thrombin was unaltered by these additions. The results so far obtained point to a deficiency of prothrombin accelerator in the patient's plasma. The concentration of this factor was determined with an assay procedure (Fantl, 1954*a*). Stored plasma free of prothrombin accelerator was the source of prothrombin. The results are plotted in Figure IV.

The results given in Figure IV show that the prothrombin of the stored plasma did not produce any thrombin at all during the period of observation, and that the addition of approximately 13% of normal Ba-plasma produced thrombin at the same rate and yield as 130% of the patient's Ba-plasma. This indicates that the concentration of prothrombin accelerator in the patient's plasma

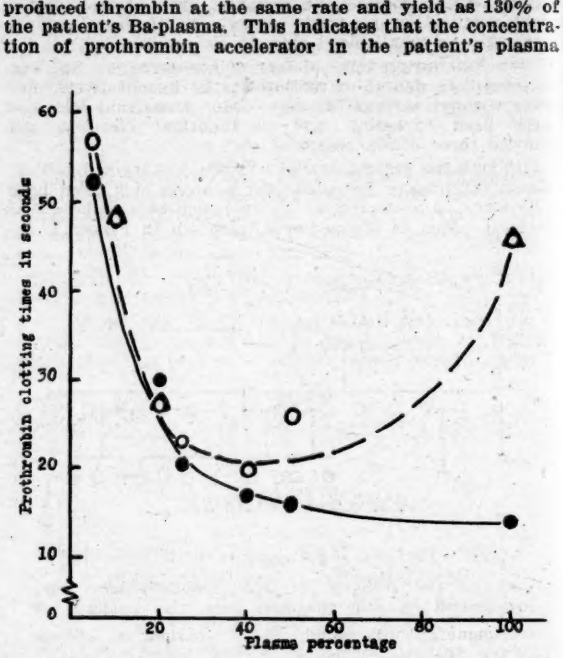

FIGURE II.

One-stage prothrombin clotting times. Curve ● — ● indicates results obtained from normal plasma. Curve ○ - - - ○ indicates results obtained from patient's plasma. Curve △ - - △ indicates results obtained from patient's plasma twenty-four hours after intravenous injection of 50 milligrammes of vitamin K_1. Dilutions were made with Ba-plasma.

is 10% of the normal concentration. The presence of prothrombin accelerator in the patient's plasma is not due to the blood transfusion given five days earlier, because the level of prothrombin accelerator and the one-stage prothrombin clotting time remained at the same level for another week.

The clotting defect could be partly and temporarily corrected by the transfusion of fresh blood, as is indicated by the experience summarized in Table IV.

TABLE III.

Prothrombin Times of Oxalated Plasma Specimens.[1]

Experiment.	Patient's Plasma.	Normal Plasma.	Patient's Ba-plasma.	Normal Ba-plasma.	Normal Stored Plasma.	Patient's Serum.[2]	Normal Serum.[2]	Clotting Time. (Seconds.)
I	0·1	—	—	—	—	—	—	31 to 60
II	—	0·1	—	—	—	—	—	10 to 12
III	0·04	—	—	0·06	—	—	—	22
IV	—	0·04	—	0·06	—	—	—	17
V	0·06	—	—	—	—	—	0·04	16
VI	—	0·06	—	—	—	—	0·04	11 to 13
VII	—	—	—	0·05	0·05	—	—	41
VIII	—	—	0·05	—	0·05	—	—	70
IX	0·05	—	—	—	0·05	—	—	39
X	—	0·05	—	—	0·05	—	—	23
XI	—	0·06	—	—	—	0·04	—	14·5

[1] To 0·1 millilitre of plasma was added 0·2 millilitre of a mixture containing equal volumes of 6% human brain extract in 0·15M sodium chloride solution and 0·01M calcium chloride solution at 37° C.

[2] The sera were obtained from blood kept at 20° C. for twenty-four hours, after which the clot was removed.

The results given in Table IV were obtained before and two and a half hours after a direct transfusion of 650 millilitres of blood. The patient weighed 52·2 kilograms and her blood volume was assumed to be five litres. Testing a mixture of 10% normal plasma and 90% of the patient's plasma before the transfusion gave a prothrombin clotting time of twenty-four seconds. After the transfusion of approximately 13% of fresh blood the prothrombin clotting time was twenty-one seconds, which is in fair agreement with that obtained *in vitro*. This would indicate that the prothrombin accelerator present in the transfused blood was distributed in the assumed blood space. It may be pointed out in passing that such behaviour is not found after the transfusion of blood or blood products in prothromboplastin deficiencies, in which large losses of the transfused factor occur immediately after transfusion (Fantl and Sawers, 1954).

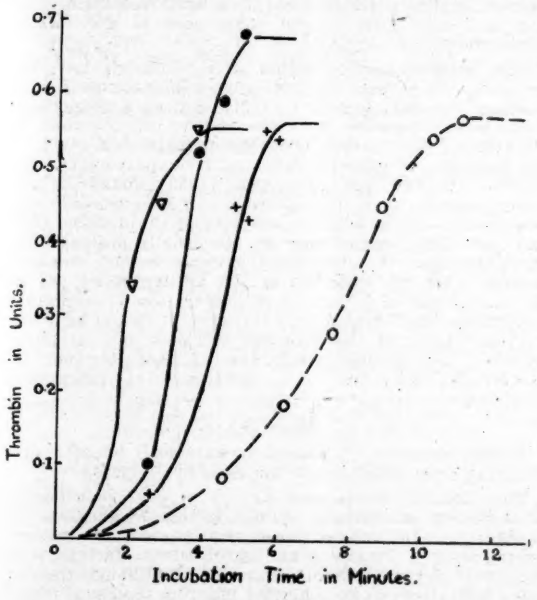

FIGURE III.

Rate of thrombin formation. (i) Curve ○ - - - ○ indicates patient's oxalated plasma obtained five days after transfusion of five pints of blood. (ii) Curve + — + the same as (i) *plus* 0·2 millilitre of normal Ba-plasma. (iii) Curve ▽ — ▽ the same as (i) *plus* 0·02 millilitre of normal prothrombin-free serum. (iv) Curve ● — ●, normal oxalated plasma. In each case 0·015 millilitre of the plasma under investigation was present in the reaction mixture of 1·8 millilitres. The thromboplastin preparation was a 6% saline extract of acetone-extracted dried human brain. The thrombin concentration was determined in 0·2 millilitre aliquots, and the corresponding units are recorded.

In addition to the experiments in which plasma was used, the influence of serum on the clotting process was also investigated. It was noted that normal serum accelerated the thrombin formation in the patient's plasma in the one-stage test (Table II) as well as in the assay procedure (Figure III). These observations made it desirable to determine the activity of the factors present in serum which accelerate prothrombin conversion into thrombin, and which have been variously called SPCA (Alexander *et alii*, 1950), factor VII (Duckert *et alii*, 1951), convertin (Owren *et alii*, 1951) and cothromboplastin (Mann *et alii*, 1951). Relevant results are given in Table V.

The results shown in Table V indicate that the prothrombin clotting times of the patient's serum obtained during two hours after clotting took place were considerably shorter than that of the original plasma. However, twenty-four hours later prothrombin was absent. In contrast to these results, the assay of serum prothrombin level showed a fall of the prothrombin concentration progressing with time. These results were obtained only during the

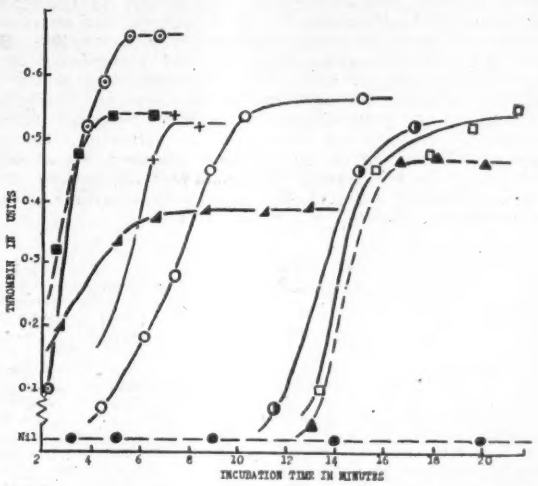

FIGURE IV.

Prothrombin activation in plasma stored for one month at room temperature. (i) Curve ● - - - ●, 0·015 millilitre of stored normal oxalated plasma. (ii) The same as (i), *plus* 13% normal Ba-plasma (□ —□). (iii) The same as (i) *plus* 26% normal Ba-plasma (◑ — ◑). (iv) The same as (i) *plus* 130% normal Ba-plasma (+ — +). (v) The same as (i) *plus* 130% normal serum (■ - - ■). (vi) The same as (i) *plus* 130% patient's Ba-plasma (▲ - - ▲). (vii) The same as (i) *plus* 130% patient's serum (◢ — ◢). (viii) Curve ○ — ○, 0·015 millilitre of patient's plasma. (ix) Curve ⊙ — ⊙, 0·015 millilitre of fresh normal plasma. The sera were kept for twenty-four hours at 20° C. Other experimental conditions were the same as those given in Figure III.

early hospitalization of the patient. With the deterioration of the patient's condition her serum contained considerable quantities of prothrombin and only small amounts of SPCA in twenty-four hour old specimens. The results given in Table IV can best be explained by the assumption that during the clotting process an activator was produced,

TABLE IV.

Influence of Fresh Blood on Prothrombin Accelerator Deficiency.

Relation to Transfusion.	"Prothrombin" Clotting Time in Seconds. (One Stage).	Thrombin Formation (Assay Procedure).	
		Maximal in Minutes.	Yield in Units per Millilitre of Oxalated Plasma.
Before transfusion	32	16	310
After transfusion ..	21	9	330
Normal	12·5	6	380

and that although it considerably improved the "prothrombin" clotting time, it did not influence the thrombin yield. However, there is an unusual feature in these serum experiments. Whereas sera taken during a period of two hours after clotting shortened the prothrombin clotting times and corresponded in the SPCA test to an

activation of 75%, the serum obtained twenty-four hours after clotting produced only 15% activation. This is in considerable contrast to the behaviour of normal serum activators (SPCA), which remain in serum for several days. An investigation of the activity of the serum prothrombin accelerators indicated that normal serum removed after twenty-four hours from the clot kept at 20° C. showed greater activity in the rate of thrombin formation of prothrombin in stored plasma than an equal volume of fresh Ba-plasma (Figure IV, curves ■ – – ■, + — +). This is probably due to the presence of prothrombin accelerator and SPCA in serum. The patient's serum showed some activity in accelerating thrombin formation of prothrombin in stored plasma, which amounted to 66% of the possible activation (curve ◢ — ◢). This corresponds to approximately 2% to 5% accelerator in her serum. The death of the patient prevented a further study of this unexpected behaviour of the prothrombin accelerators in her serum.

TABLE V.

Prothrombin of Plasma and Serum and SPCA Results.

Material Tested.	Prothrombin Clotting Time in Seconds.	Prothrombin. (Units per Millilitre.	SPCA Tests.	
			Time in Seconds.[2]	As Percentage Activation.[2]
Patient's plasma:				
100%	30	310	—	—
50%[1]	20·5	310	—	—
Patient's serum 50%[1]:				
Half an hour after clotting	15·5	240	35	33
1 hour after clotting	14·5	165	34	74
2 hours after clotting ..	17	87	37	70
24 hours after clotting ..	>120	0	45	15

[1] Diluted with Ba-plasma.
[2] SPCA test of De Vries *et alii* (1949).
[3] Calculated from the prothrombin assay and compared with a prothrombin clotting time curve of diluted normal plasma.

Discussion.

The hæmorrhagic disease of this patient has been shown to be due to a severe deficiency of the plasma factor prothrombin accelerator. The condition was not apparent before her sixth decade. Yet in view of some indications of a bleeding tendency in several of her relatives, it was considered possible that the bleeding defect was inherited. The blood of some relatives was therefore examined, but with a negative result. The mode of inheritance, if indeed it did exist, could not be demonstrated. Although no clotting data are available of the patient's blood prior to her admission to this hospital, it is fairly obvious that she could not have had a severe hæmorrhagic tendency which had gone unnoticed for over sixty years, for during this time the patient had three uneventful confinements and several dental extractions, and certainly was subjected to other traumata. It is possible that the patient's blood had a low normal prothrombin accelerator concentration before the tuberculous lesion gave severe clinical symptoms, and perhaps the infection precipitated the appearance of a prothrombin accelerator deficiency.

With regard to the procedures required to establish the laboratory diagnosis, it was found that by the one-stage test a severe prothrombin accelerator deficiency was more easily detected than by the assay procedure; but the results of the one-stage test might give the impression of a true prothrombin deficiency. On the other hand, the assay procedure gave a good indication of the rate of thrombin formation, and although this was considerably delayed, the yield of thrombin was maximal and normal, and thus excluded a prothrombin deficiency.

In addition to the prothrombin accelerator deficiency, the patient showed another anomaly. Although her fresh serum was active in accelerating prothrombin conversion of normal plasma in the SPCA test of de Vries *et alii* (1949), this activity disappeared twenty-four hours after clotting. It was established that the shorter prothrombin clotting time of the patient's serum taken soon after clotting was not due to a prothrombin concentration higher in serum than in plasma, but to development of an accelerator which showed limited stability. On the other hand, her twenty-four hour old serum did contain prothrombin accelerator activity equivalent to between 2% and 5% of the normal. A similar phenomenon may have occurred in the patients studied by de Vries *et alii* (1949) and by Kingsley (1954). The latter worker believed that the serum prothrombin accelerator was destroyed enzymatically. Perhaps the disappearance of SPCA in serum is connected with a low concentration of the plasma prothrombin accelerator.

The patient's hæmorrhagic condition deteriorated during the treatment with streptomycin and isoniazid. There is no evidence that these drugs influenced the clotting process. However, it has been suggested that isoniazid reduces capillary resistance (Merk and Weinreich, 1954), and this may have played some part in the terminal hæmorrhages.

The hæmorrhages occurring in tuberculosis have been connected by several workers with a derangement of the clotting process. Savacool (1941) noticed a reduction of prothrombin parallel with the degree of toxæmia, but vitamin K_1 had no effect on the prothrombin level. In the majority of patients suffering from pulmonary tuberculosis, Jürgens and Staamann (1950) found hypoprothrombinæmia, even in the absence of hæmoptyses, which was again parallel with the severity of the disease. Saito and Abo (1952) found that the abnormally prolonged prothrombin time of tuberculous patients became gradually shorter after the injection of 100 milligrammes per day for four weeks of a vitamin *K* preparation (2 methyl-1, 4-naphtho-quinone-bisulphite). However, it should be pointed out that none of the previous workers has established whether the clotting defect was in fact due to hypoprothrombinæmia or to a deficiency of prothrombin accelerator.

Summary.

A fatal hæmorrhagic disease in an elderly female patient suffering from tuberculosis has been investigated.

The clotting defect was due to a 90% deficiency of prothrombin accelerator (labile factor, Ac-globulin, proaccelerin). In contrast to normal serum, the patient's serum showed limited stability of serum factors which accelerate the prothrombin conversion. Although there are some indications of an inherited bleeding tendency, none of the relatives of the patient who were examined have shown a clotting deficiency, and it is believed that the patient's hæmorrhagic disease was acquired.

Acknowledgements.

Our grateful thanks are extended to Dr. J. E. Sewell, honorary in-patient physician at this hospital, by whom the patient was referred to us, and to Dr. A. V. Jackson, who carried out the post-mortem examination.

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Reviews.

CORRIGENDUM.

THREE errors appear in the review of "The Distribution of the Human Blood Groups", by A. E. Mourant, which was published in the issue of March 10, 1956, at page 408. In the second column, line 19, the lower case "s" in "MNSs" should be omitted, so that the phrase will read: "the MNS blood groups". In line 20 and again in line 49 of the same column a comma should be inserted between "P." and "Lutheran", so that the phrase will read "the P., Lutheran, Kell, Duffy" *et cetera*.

Advances in Pediatrics. Edited by S. Z. Levine, with associate editors John A. Anderson, Margaret Dann, A. Ashley Weech, Myron E. Wegman and Warren E. Wheeler; 1955. Chicago: The Year Book Publishers, Incorporated. Volume VII.

THIS seventh volume of the series will be welcomed by pædiatricians. The authoritative and up-to-date reviews maintain the high standard of previous volumes. The seven monographs written by well-known authorities in their respective fields will interest pædiatric physicians, surgeons and radiologists. John Caffey's monograph on fibrous defects in cortical walls of growing tubular bones indicates careful and detailed radiological study over a considerable period of these interesting changes. A long, thorough and detailed review of the urinary tract in childhood is presented by Meredith Campbell. Phonocardiography in children by Mannheimer, of Stockholm, is a topical subject, clearly presented. Meyer Perlstein's name is well known in the field of cerebral palsy, and his clear presentation of all aspects of infantile cerebral palsy and review of recent literature will be helpful to all practitioners meeting this problem. Shwachman and others from the Children's Medical Center, Boston, write an extensive and thorough review of mucoviscidosis and present their reasons for preferring this title to the more familiar one of fibrocystic disease of the pancreas. Of particular interest is their discussion upon partial pancreatic insufficiency with their review of the probable important place of the estimation of sweat electrolytes in the diagnosis of this condition. Orvar Swenson gives an excellent brief review of congenital megacolon. He emphasizes the serious but unusual features of gastroenteritis in these children. Perhaps the review of least interest in this country is that of Gomez *et alii* upon malnutrition in infancy and childhood, with special reference to kwashiorkor. It is based on Mexican experience and is a reminder of the extensive problems of severe malnutrition which exist in the world today.

Lunacy, Law and Conscience, 1744-1845: The Social History of the Care of the Insane. By Kathleen Jones, Ph.D.; 1955. London: Routledge and Kegan Paul, Limited. 8½" × 5½", pp. 266. Price: 21s.

THE time is ripe for a review of the social history of the care of the insane. In the century preceding 1845, Kathleen Jones has in "Lunacy, Law, and Conscience" given an admirable account of this period, aptly termed the first stage of the revolution in mental therapy. The reader will see in clear perspective the long fight against public apathy which permitted unbelievable hardships for those afflicted with mental disorders.

The introductory chapters deal with eighteenth century practice, including the woes and horrors of Bedlam and the parallel "frugality of management" in the workhouses and poorhouses.

Many of the insane spent their time in Bridewells or houses of correction, which differed little from gaols. Few records were kept and fewer have survived. The author skilfully pieces together the shreds of evidence, largely taken from commissions, to produce a coherent account.

Woven into the story, as a contrast to the foul linen and stinks of the unwashed, is a golden thread of human kindliness, which as the years pass grows in size and vividness. The commonplace of clouds with silver lining is shown in the results which stemmed from the mental illness of King George III. Gradually the public conscience was aroused to full realization of the problem, and in the century under review there was created the basis of sound treatment for the afflicted. A thorough inspection of hospitals was initiated, and the adequate housing of lunatics became an accepted responsibility of the government.

Dr. Jones shows that the happy ending was achieved through the indefatigable labours of a small band of

reformers. A sixty-year-old high sheriff, Sir George Onesiphorus Paul, in 1806 drew attention to the hard lot of pauper lunatics. In 1813 Godfrey Higgins, gentleman, wrote to the Press concerning the "Augean Stables" of the York Asylum. It resulted in bitter controversy which led to inquiries that touched every aspect of the problem in hospitals, gaols and poorhouses. Records were burned, reputations were smirched, and the guilty were sacked. The outstanding work of Ashley in steering reform through the devious channels of Parliament is clearly described. Space will not permit review of the complicated steps which led to a happy ending. It makes interesting reading even for those with a scanty knowledge of psychiatry, and is a reminder of the need for patience and perseverance in the prosecution of reform.

The appendix includes a valuable section on criminal lunatics, and an account of the events which led to the well-known "McNaughton Rules". Seen in historical perspective they are a credit to the fundamental fairness of British law.

"Lunacy, Law, and Conscience" is worthy of a place, not merely in the library of every psychiatrist, but also on the bookshelves of those who are interested in sociology or law.

Notes on Books, Current Journals and New Appliances.

The M.B., B.S. Finals: A Collection of the Papers Set at the London M.B., B.S. Examination for the Years 1946-1955, Classified and Arranged in Suitable Sub-divisions, by Francis Mitchell-Heggs, T.D., M.B., B.S. (Lond.), F.R.C.S. (Eng.), F.R.C.S. (Edin.); Fourth Edition; 1955. London: J. and A. Churchill, Limited. 8" x 5¼", pp. 88. Price: 10s. 6d.

"THE M.B., B.S. FINALS" has now been issued as the fourth edition. It consists chiefly of the questions set for written reply in the final M.B., B.S. examinations of the University of London during the years 1946 to 1955. The advisability of revising or of learning medicine in this way is open to comment, though it may comfort the student to know that the questions are rarely abstruse. It may also help him to practise the written answers to questions, if this method is still unfamiliar by the time that he reaches the final examinations. This book will also be of interest to the graduate who wishes to review his past knowledge of the fields of medicine which have become unfamiliar. The first part of the book consists of a final prospectus of study, requirements for entrance to the examinations and facilities for clinical work available in the University of London academic area. Neither the regulations nor the form of the final examination are the same for the other English universities. The questions are arranged with some skill into both subject and type. It is surprising to note that there is no separate section for pædiatrics, but otherwise the main branches of medicine are well covered. The student of any university will find that the foreword contains some excellent advice.

Dried BCG Vaccine, by Yoji Obayashi; 1955. Geneva: World Health Association (Monograph Series, Number 28). 9¼" x 6¼", pp. 220. Price: £1 5s.

THIS monograph by Dr. Y. Obayashi, Assistant-Chief of the Research Department of the Japan Anti-Tuberculosis Association, describes in detail the extensive experiments which have been conducted in Japan to produce on a large scale a stable and potent B.C.G. vaccine by the method of freeze-drying. Difficulties and disappointments were encountered when experimental methods were translated into mass production, but these have been overcome up to a point. The vaccine now being produced, containing less than 3% of moisture and dispensed in evacuated sealed tubes, keeps for long periods under refrigeration, and its potency, assayed before release, can be relied upon much more than that of liquid vaccines. The author states that B.C.G. vaccine at present being produced in Japan cannot be said to meet all the requirements of a satisfactory vaccine for large-scale use in the field. For example, it has not yet been developed to the point at which it can safely be preserved at room temperature in summer, though it is not certain that this will ever be possible. The monograph will be of interest to those who have encountered and overcome similar problems and difficulties in this country and those who work in this field. A French translation of the monograph is in preparation.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Cancer and Allied Diseases", by Ronald W. Raven, O.B.E., T.D., F.R.C.S.; 1955. Modern Health Series. London: Gerald Duckworth and Company, Limited. 7½" x 5", pp. 106. Price: 8s. 6d.

Written for the general public.

"Childbirth", by W. C. W. Nixon, M.D., F.R.C.S., F.R.C.O.G.; 1955. Modern Health Series. London: Gerald Duckworth and Company, Limited. 7½" x 5", pp. 106. Price: 8s. 6d.

Written for the general public.

"The Lacrimal System", by Everett R. Veirs, M.D.; 1955. London and New York: Grune and Stratton. 10" x 6¾", pp. 168, with 68 illustrations. Price: $7.50.

The author deals with the whole lachrymal system and lays stress on forms of treatment and operations which "have stood the test of time".

"James Parkinson, 1755-1824: A Bicentenary Volume of Papers Dealing with Parkinson's Disease, including the Original 'Essay on the Shaking Palsy'", edited by Macdonald Critchley, with the collaboration of William H. McMenemy, Francis M. R. Walshe and J. Godwin Greenfield; 1955. London: Macmillan and Company, Limited. 7" x 5", pp. 284. Price: 15s.

J. G. Greenfield writes on the pathology of Parkinson's disease and F. M. R. Walshe on a clinical analysis of the *paralysis agitans* syndrome.

"Any Hope, Doctor", by Irene Gates, M.D.; 1955. London: Blandford Press. Melbourne: M.R.A. Books. 7½" x 5", pp. 203. Price: 10s. 9d.

The story of a woman doctor and how she dealt with crises in the lives of men and women and was able to help them.

"Of Research People", by George E. Burch, M.D., F.A.C.P.; 1955. New York and London: Grune and Stratton. 10" x 8", with 40 illustrations.

A serious essay with some delightful satirical illustrations.

"Elementary Physics", for medical, first year university science students and general use in schools, by G. Stead, M.A. (Cantab.), D.Sc. (London), F.Inst.P.; Ninth Edition; 1955. London: J. and A. Churchill, Limited. 8½" x 5¾", pp. 548, with 448 illustrations. Price: 21s.

The first edition was published in 1924.

"The Relief of Symptoms", by Walter Modell, M.D., F.A.C.P.; 1955. London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. 9" x 6¼", pp. 459. Price: £4.

The book is "offered as a practical guide to the problems of providing the patient with relief from his distress".

"Neural Control of the Pituitary Gland", by G. W. Harris, F.R.S., Sc.D., M.D.; 1955. London: Edward Arnold (Publishers), Limited. 8½" x 5½", pp. 297, with illustrations. Price: 30s.

Intended for the student "who will, within the course of a few years, be standing on his own feet in the research field".

"An Atlas of Bone-Marrow Pathology", by M. C. G. Israëls, M.Sc., M.D., F.R.C.P.; Second Edition; 1955. London: William Heinemann (Medical Books), Limited. 9¾" x 7¼", pp. 95, with 13 plates. Price: 30s.

The first edition appeared in 1948.

"Modern Public Health for Medical Students", by I. G. Davies, M.D., F.R.C.P., D.P.H.; 1955. London: Edward Arnold (Publishers), Limited. 8½" x 5½", pp. 494. Price: 30s.

An attempt "to show the significance and importance of the community aspects of ill-health, and to teach the purpose of the legislative, administrative and social measures" adopted by the State.

The Medical Journal of Australia

SATURDAY, MARCH 31, 1956.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words of phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

HEALTH CENTRES.

AMONG the provisional aims of the *National Health Service Act*, 1946, of Great Britain, was the setting up of health centres. We all know that not much success in this direction has been achieved, and the subject has been discussed on more than one occasion in these columns. It will be useful to remind readers of the ideas that lay behind the provision of health centres. They are discussed in Stephen Taylor's book entitled "Good General Practice", which was mentioned at some length in these columns in the issue of September 25, 1954. Taylor pointed out that the legal definition of a health centre had been deliberately drawn wide, so as to make possible a variety of experiments. Legally, he wrote, a health centre could be a building which included general practitioners only with no health authority clinics or other services. In other words, local health authorities were empowered under *The National Health Service Act* to provide group practice centres as well as health centres proper. Taylor gave the following "functional definition" of a health centre: "Apart from the questions of ownership, a health centre is a building where the GPs carry out their work under the same roof as the local authority health services." Its essential feature is that the therapeutic service provided by the general practitioner and the preventive service of the local authority are brought together. Taylor pointed out that his definition contained the idea behind the conception of health centres, and he thought that as a means of bridging the gap between the two services mentioned, it was sound. He added that this was only part of the story. The local authority clinics had grown up because the general practitioners could not provide a service without fee for expectant and nursing mothers and young children. Under the *National Health Service Act* the general practitioner could be paid such a fee. Taylor had found in the survey on which his book was based that the good general practitioner was often running an efficient ante-natal and post-natal scheme for his patients, usually with full cooperation from the midwife. As a result of this, in a few places official and ante-natal clinics had had to be shut down for want of support. Taylor concluded that the conception of a health centre would be determined by the future of the ante-natal clinics. With our discussion in September, 1954, of Taylor's book, reference was made to a report on the Committee on General Practice within the National Health Service. In this report, the number of health centres which had been established was referred to, and it was stated that only four had been established since 1948. *The Times*, it was noted, had discussed the case for group practice, and added that the committee's report probably marked the final burying of the health centre idea, save for an occasional experiment in unusual circumstances. Taylor stated that, at their best, health centres were an untried solution, while for economic reasons they could not become general for many years. This, of course, supported the contention of *The Times*. Taylor stated that the administrative difficulties encountered by those trying to create and staff health centres in areas of established practice had been very great. He saw no reason why the general practitioners in a group practice building should not provide accommodation which could be let to and used by the local health authority for clinic and other purposes. In this way, a group practice centre could become a health centre in function, if not in name or law. He referred to the small "health centre" at Harlow New Town, and stated that it approximated closely to the conception he had mentioned. The building was owned by a neutral landlord, the Development Corporation. The three general practitioners in group practice, the two dentists in general dental practice, and the local health authority were all there as tenants of the Corporation. He stated that a sound symbiotic relation had been achieved through physical proximity alone.

It might be of interest to refer to what was known as the "Peckham Experiment". This was described in a book published by I. H. Pearse and L. H. Crocker, published in 1943, and reprinted in 1944. A great deal was expected from what was done at Peckham, and what Pearse and Crocker wrote was certainly stimulating. Eventually, however, an announcement was made that the Peckham Experiment had been abandoned, and this was discussed by M. R. A. Chance in *The Lancet* of April 15, 1950 (see THE MEDICAL JOURNAL OF AUSTRALIA, August 12, 1950, page 265). The conclusion reached in our discussion on that occasion was that probably Chance had not told the whole story of the closure of the Peckham Health Centre, and that further information would be awaited. What Australian practitioners wanted to know was whether the "Experiment" had really failed.

No sensible person will dispute the claim that the establishment of health centres and their proper functioning would be to the advantage of medical practice and of benefit to the community. Clearly, Stephen Taylor put his finger on a vital point when he referred to the difficulty of establishing health centres in areas which were already being served by practitioners in private practice. His suggestion that practitioners in a group practice might by letting accommodation to the local health authority create a health centre in function, if not in law, was worthy of

serious consideration. Ideally, a health centre could best be established in an area which was gradually becoming populated, so that the health centre would grow as the community grew. This has been possible at the new town of Harlow, just outside London. What has been achieved was described in *The Lancet* of October 22, 1955, by Stephen Taylor, who is a visiting research fellow of the Nuffield Provincial Hospitals Trust and a member of the Harlow Development Corporation. As co-authors, he had six general practitioners of Harlow New Town, three dental surgeons of Harlow New Town, a county medical officer of health of Essex, and an area medical officer of the Essex County Council. This venture has been made possible by the initiative and generosity of the Nuffield Provincial Hospitals Trust. In October last three centres had been finished, and the last of these was officially opened by Lord Nuffield. Harlow is one of eight new towns around London which are being built in order to relieve the metropolis of some of its excess population. The people of Harlow are thus primarily Londoners, particularly North Londoners, who come out with their industries. When a factory moves to Harlow, its employees are given the chance to come, and as a result more than three-quarters of the men with their families decide to make the move. The result is that most of the families in Harlow consist mainly of young persons. Many of them have never had a home of their own before. A popular newspaper once referred to Harlow as "Pram Town—where there's a hole in every pocket, and a smile on every face". This is not completely true, according to Taylor and his colleagues, because some of the families feel the result of financial stress, and what are described as justifiable anxiety states make their appearance. About four years ago, when the temporary health centre was opened, New Harlow had about 700 houses and flats occupied, and its population was 2500. Last October about 6400 houses and flats were occupied by over 22,000 new residents. It is expected that by 1958, over 12,000 houses and flats will have been completed, housing over 40,000 persons. The town will then have passed its half-way mark towards its ultimate target of 80,000. For a practitioner to "squat" in the new town of Harlow has, we are told, been more than an act of faith—it needed courage and the financial strength to exist until one's practice had been "clothed by the Development Corporation's housing". At first the area was what is known under the National Health Service of Great Britain as an open practice area. This meant that a practitioner would receive a certain basic salary while his practice was growing. So many private practitioners have started that the area is now a "Schedule-2" or intermediate area. This means that new doctors are warned that their chances of list-building are limited, and no basic salary is available during the initial years of practice. In completely new towns and housing estates the Government enforces the regulation by which it controls property use, and this control is exercised by the estate authority. This means that no dwelling houses may be used for the practice of a business or profession, and no professional or business plate, notice board or sign may be erected. In other words professional people may not conduct practices from Corporation dwellings. Of course, the Corporation cannot control what happens in premises which it does not own. Most of the doctors in the new town, therefore, either have selected themselves by opening up in private premises, or have started as outposts of existing partnerships in the old town or elsewhere. Once they have established themselves in New Harlow and have acquired enough patients to show that they are there to stay, the Corporation has done its best to help them to serve their patients.

Some of the principles of the "treaty-making" of the centre and the principles adopted in practice are of interest. The principles of tenancy have been devised to achieve (*inter alia*) the following objectives: (i) To give reasonable safeguards to the doctors who enter the health centres against the consequences of so doing. (ii) To give a reasonable assurance to the public that in any area there are enough doctors, and that there is a reasonable choice of doctors. (iii) To insure that the conditions inside the health centre are in accord with the purpose of providing a demonstration of good general practice. (iv) To make sure that assistants-with-a-view and junior members of partnerships are fairly treated. It is thought that assistants-with-a-view and junior partners should be fairly treated over night work, week-end duties and holidays, but at the same time, in return for the generous treatment that they receive, it is expected that the younger members of a partnership will willingly carry rather more than their share of the work burden to help the seniors in the fifties and sixties. The actual conditions of tenancy include the following: (i) Consulting rooms with the use of all other necessary facilities are let to individuals or partnerships. (ii) Before a tenancy to a partnership is granted or extended, the partnership agreement must be approved by the Nuffield Trust. (iii) The agreement is also required to be approved by the Medical Practices Committee and a certificate obtained under Section 35 (9) of the *National Health Service Act*, 1946. Leases to principals or partners are made for twenty-one years or less if desired, with the option of renewal for a further period of twenty-one years or less, the rent on renewal to be subject to negotiation. (iv) A doctor practising from a health centre is not allowed to conduct a regular surgery or exhibit a plate or board elsewhere in the area of the new town served, or to be served, by one of the Trust's health centres. (v) If a partnership fails to grow to meet the medical needs of an area, the Nuffield Trust retains the right to let vacant consulting rooms to doctors not in partnership with those already in the health centre.

The health centres at Harlow, we are informed by an editorial, do not comply with the full conditions of health centres according to the terms of the *National Health Service Act*. What is important, however, is that health authorities and general practitioners are working in the same centre, and that apparently a considerable degree of cooperation is achieved. Stephen Taylor and his colleagues state at the beginning that their article not only tells of the planning and building of the three centres in use, but also gives important lessons in human relations and cooperation. Under conditions existing at Harlow cooperation of the medical attendant or clinical doctor and the official health doctor would, we should think, be difficult to avoid. With this kind of achievement in a new and growing community as an example, it should surely not be beyond the ability of practitioners of preventive and curative medicine, even in this country, to come closer together than they do.

Current Comment.

THE CONTROL OF VIRUS DISEASE

LINES of reasoning based on three groups of data relating to certain phenomena of virus behaviour have led F. L. Horsfall, junior,[1] to reach an interesting conclusion about the possibility of controlling virus infections. Taking, first, the behaviour of the yellow fever virus, Horsfall describes the course of events as follows: when an infected mosquito bites a man, a minute number of virus particles are injected. These promptly leave the blood-stream and invade selected cells in the liver, lymph nodes and kidneys. During the next four days reproduction of virus goes on within the infected cells; at the end of that period enormous numbers of virus particles have been released from the cells, and the symptoms of yellow fever appear. Thereafter the concentration of particles in the blood rises, and may reach the figure of 100,000,000 per millilitre. By about the fourth day of the disease, however, neutralizing antibodies make their appearance, and as they increase so the number of particles decreases, until the rate of neutralization of virus becomes greater than the rate of production of virus, and then the number of particles falls off rapidly. It is not, however, the presence of virus particles in the blood which causes the signs and symptoms of the disease; these are due to the number of cells damaged by the reproductive processes of the virus. Nor is the disease cured by the neutralizing antibodies directly—production of virus, having reached its peak, must fall off quantitatively, as the number of cells put out of action, and therefore rendered unavailable for virus reproduction, increases. Nevertheless, antibodies play some part by neutralizing virus before it can reenter unaffected cells. However, the progress and outcome of virus disease seem to depend rather on two numerical factors directly concerned with the virus: first, the number of particles initially injected, and second, the rate of reproduction of the particles; added to this are two numerical factors directly concerned with the host: the number of suitable cells available for virus reproduction, and the rate of regeneration of these cells.

The conception that virus disease is a quantitative phenomenon, depending upon the numbers of susceptible cells in any given system which are put out of action by the processes of virus reproduction, is an important one. It has been shown that a single particle of vaccinia, or of influenza virus, can produce disease in experimental animals. It is known that some viruses reproduce, during each intracellular cycle, at rates of the order of ten, while others reproduce at rates much higher than a thousand; thus three cycles of the former would result in the formation of 1000 new particles, but three cycles of the latter would produce 1,000,000,000 new particles. Moreover, some viruses have short reproductive cycles, while others have long ones. There is also evidence that a particular virus can vary in these two factors—that so-called avirulent or attenuated strains have a lower and slower rate of reproduction than virulent strains; but this may be rather an expression of the factor of suitability or susceptibility of the host cells. For instance, a virulent strain of influenza virus can cause disease in man, or in the ferret; but although it will multiply in the mouse, it must undergo a process of adaptation before it will reproduce the disease in that animal. Furthermore, a virulent strain of mumps virus from man will multiply in the chicken embryo, but no adaptation takes place, and the chicken embryo suffers no apparent damage or disease. Similarly, the yellow fever virus, which multiplies in the mosquito's cells, and which, after some twelve days, becomes infective for man, causes no damage or disease in the mosquito.

Returning now to the matter of neutralizing antibodies: Horsfall suggests that antibodies against viruses are short-lived, and that continued immunity against a virus is dependent on a continuing low-level infection by the virus. Antibodies do not reach, and therefore do not neutralize, the intracellular particles, but only those that enter, and remain for a time in, the blood-stream. This suggests a further quantitative reaction, in which antibodies develop in response to the presence of virus particles in the blood, but only in sufficient amount to neutralize the particles present, without the formation of a considerable surplus. This would explain why pooled adult serum (containing minute amounts of antibody) may, if given just prior to exposure to infection by measles, protect a child from being infected, whereas no amount of serum will effect a cure once measles (or any other virus disease) has developed. There may be enough antibody to neutralize the few infecting particles, but it is not nearly enough to cope with the vast numbers of particles produced when the disease has developed fully. Horsfall's suggestion can also explain why there is only a transitory immunity following influenza and certain other respiratory or gastro-intestinal virus infections; since these are essentially infections of surface cells which are thrown off as soon as they become damaged, there can be no continuing infection to stimulate continued antibody formation—if, indeed, any considerable numbers of virus particles from such infections ever enter the blood-stream. It is more likely that in these conditions (as in *herpes simplex* and psittacosis, recovery from which is not accompanied by any measurable rise in antibody formation) the virus ultimately runs out of suitable cells in which it can reproduce, and so dies out.

All this raises the question of suitable and susceptible cells. For this aspect Horsfall goes first to the bacteriophages. A single phage particle can infect a bacterium; the tail of the particle penetrates the wall of the bacterium, and then the head-contents (nucleic acid of the desoxyribose type) enter the bacterium. At this stage the shell of the head and external portion of the tail of the phage particle can be removed without interference with future processes. Shortly after, the bacterium stops synthesizing bacterial components and produces phage nucleic acid and phage protein (separately, not as complete phage particles). After a time, tailless heads (protein shells) appear in the bacterial cytoplasm; later a tail is added and the particle fills with nucleic acid. The bacterium then disintegrates, and over 100 new phage particles are released, to attack other bacteria. Now, chloramphenicol and certain analogues of tryptophane inhibit protein synthesis in bacteria, while certain pyrimidine analogues inhibit nucleic acid synthesis in bacteria, and when exhibited during the phases of production of these substances, they inhibit phage reproduction. Furthermore, proflavine (which does not interfere with synthesis of either protein or nucleic acid) prevents the final assembly of the phage particles, so that only tailless heads are produced.

Comparing these phenomena with those of animal viruses, Horsfall points out that there have been no essential differences so far discovered. Animal virus particles have no tails; their shells are composed of a protein, and while some contain nucleic acid of the desoxyribose type, others contain the ribose type and some contain both types; some have central dense areas resembling nuclei. Whether the whole particle enters the host cell has not been determined; at any rate, after it has attacked a cell all trace of it is lost for a time, and nothing is known of what goes on until formed elements resembling virus particles appear in the cell cytoplasm. However, many animal viruses do not cause destruction and disintegration of the host cell, presumably because their demands on cell synthesis are not at variance with the cell's normal synthetic programme. Now, certain analogues of amino acids, such as methoxinine and ethionine, inhibit protein synthesis in cells, and when applied early in the period of eclipse of the invading particle they inhibit the development of influenza and poliomyelitis reproduction. Similarly 2,6 diaminopurine inhibits nucleic acid synthesis, and also the reproduction of vaccinia and some encephalitis viruses. Acridine and certain glycosides of benzimidazole inhibit mumps and influenza. From this

[1] *Canad. M. A. J.*, November 15, 1955.

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evidence it can be reliably assumed that the unknown intermediate processes which go on in animal viruses are closely analogous to those of bacterial virus reproduction.

It would seem then that some cells are suitable vehicles for virus reproduction because their synthetic processes are capable of producing virus protein and virus nucleic acid; in some of these suitable cells, because their synthetic process closely parallel those of the viruses, little damage results from the invasion, while in others the demands of the virus wrench the synthetic processes aside and result in destruction of the cell.

The only difficulty is that the substances which can inhibit the synthesis of essential elements of the virus particles must be applied very early in the course of the infection (ideally, before infection occurs, in which case they must be of a nature to remain in the tissues for long periods); they must also, of course, be safe for the tissues and their normal synthetic processes. Horsfall concludes that it must eventually be possible to find compounds which are non-toxic, and are sufficiently potent to inhibit virus reproduction early in the incubation period. This must be so, if it is conceded that the presence of virus particles in the blood is not the disease itself, but that the damage the particles do during their reproductive cycle inside suitable and susceptible cells causes the signs and symptoms of the disease.

THE TREATMENT OF PEMPHIGUS WITH CORTISONE AND ACTH.

THE treatment of pemphigus has been a depressing business in the past. This ill-understood group of conditions frequently issued in death or chronic invalidism, in spite of all forms of treatment; and even when recovery occurred, the real value of the particular therapy used was often questioned. The advent of cortisone and ACTH has changed this. Although they are not curative and their prolonged use brings its own problems, they have certainly brought new hope; and reports now appearing begin to make possible their long-term assessment. Experience in the treatment of 28 patients with pemphigus over a period of five years is described by C. T. Nelson and M. Brodey.[1] Of the 28 patients 27 had *pemphigus vulgaris* and one had *pemphigus foliaceus*. Two or more experienced dermatologists agreed on the clinical diagnosis before any patient was included in the study, and each diagnosis was confirmed by biopsy. All were treated with cortisone or ACTH, but cortisone given by mouth is regarded as the simplest and most satisfactory form of therapy. Of the 28 patients 21 survived, all but two being able to pursue their daily activities without serious restrictions; seven are dead. Two of the deaths resulted from major thrombo-embolic accidents during the course of treatment; the others were probably associated with inadequate amounts of hormonal treatment, as judged by present standards. Of the survivors one has maintained a state of clinical remission for twenty-five months without steroid therapy (his period of treatment lasted for six months); the remainder require maintenance hormonal treatment in varying amounts. The important point is that the periods of treatment of the survivors range from two to sixty-six months, being over five years in two cases, over four years in four, over three years in six and over two years in nine. In addition to three major thrombo-embolic episodes, two of which were fatal, the incidence of side effects was high; the most serious were psychic disturbances (seven), osteoporosis (three) and reactivation of peptic ulcer (three). Nevertheless, as Nelson and Brodey point out, in the treatment of a lethal disease such as pemphigus one cannot afford to be unduly concerned by the physiological side effects produced by hormones which control the disease. The opinion expressed in this paper is that to exert a beneficial effect on pemphigus by the use of steroids, it seems necessary to induce some measure of hyperadrenocorticalism; and the usual physical stigmata of Cushing's syndrome apparently led to little real difficulty. There is a calculated risk involved, which should be the subject of mutual understanding between doctor and patient; and the encouraging fact emerges from this long-term study that once the disease is brought under control, it is possible in nearly all cases to reduce the daily dosage of corticosteroid gradually (exceptionally to discontinue it entirely) and still maintain a remission. It remains to be seen whether the success achieved by cortisone therapy will ultimately throw any light on the causation of pemphigus.

[1] *Arch. Dermat.*, December, 1955.

GOUT AND HISTORY.

MANY famous persons of the past have suffered from gout, but it is rather startling to be told that this painful malady (perversely considered funny by some people) has influenced the course of history and tinctured the springs of literature and philosophy. However, so it would seem to be from the material gathered by Wallace Graham and K. M. Graham,[1] who quote the view of Havelock Ellis that a real association exists between gout and the genius of many of its victims. The list is impressive, even if we allow that the diagnosis is disputable in some cases: Milton, Harvey, Sydenham, Newton, Gibbon, Fielding, Hunter, Samuel Johnson, Congreve, the Pitts, Wolsey, Landor, Hamilton, Charles Darwin, Francis Bacon, Luther, Calvin, Goethe, Franklin, Sydney Smith and Queen Anne ("Brandy-faced-Nan"). The most striking story concerns Pitt, Earl of Chatham. Besides suffering from gout Pitt was afflicted with a manic-depressive condition ("euphemistically called gout in the head"). Despite failures in his early political life Pitt achieved supreme power in 1757 at the age of forty-nine years, when the Government, weary after many years of war with France, was seeking peace. Pitt opposed this, and we are given a vivid picture of him being carried to the House, ill, with his legs in rolls of flannel and his gouty foot in a vast boot, and, with the House's indulgence, sitting through part of his three and a half hours' speech. Despite his passionate pleading, he was defeated; and after the Peace of Paris he resigned his office. When the *Stamp Act* was passed in 1765 to force the American Colonies to share the cost of the war, Pitt disapproved strongly, but was too ill to make the journey to London to protest. In 1766 he recovered sufficiently to force the repeal of the Act and was given sole direction of affairs foreign and domestic. Again he collapsed, and while he was out of action the colonial duty placed on tea and other commodities led to the Boston Tea Party and rebellion. In the following year Pitt recovered sufficiently to take up America's cause, and after consultation with the colonists' spokesman, Benjamin Franklin, "another great gouty character", he introduced a compromise Bill. It was defeated, to Pitt's unutterable disgust, and again his health forced him into retirement. The inevitable sequel was war between England and America and American independence, despite the last great effort of the dying Pitt, and he did not live much longer. Trevelyan comments in his "History of England":

> The gout, which he had been fighting with heroic constancy ever since his Eton days, at last overcame the resistance of a lifetime. For months together he lay in brooding melancholy, refusing to see his bewildered colleagues, fierce and unapproachable like a sick lion in its lair. His ministry which had no principle of cohesion save his leadership staggered to ruin, carrying to limbo the last hopes of the country and the Empire.

How unfortunate for England, comment the Grahams pertinently, that colchicum was not more widely used in the time of Pitt. Perhaps, as they suggest, the responsibility for this (and so perhaps for the loss of America) belongs to the great Thomas Sydenham. Himself a sufferer from gout, Sydenham wrote the classical description of the disease in 1683; but unfortunately the great weight

[1] *Canad. M. A. J.*, September 15, 1955.

of his authority was thrown against the reintroduction of colchicum, a drug which had been known to the ancients for the treatment of gout. The fact was that he was opposed to purging (a laudable attitude to the modern way of thinking), colchicum was thought of in his day essentially as a purgative, and so he kept out of use what was (unknown to him) a specific for the disease with which he himself like many another was plagued. It is almost intolerable to speculate what might have been had his influence gone in the opposite direction. The whole pattern of the western world might have been different if Pitt and the many gouty giants of the seventeenth and eighteenth centuries had known, as even Mrs. Beeton knew in the nineteenth century and perhaps the Egyptians knew in 1500 B.C., the virtues of colchicum.

BIBLIOGRAPHY OF MEDICAL REVIEWS.

THE United States Armed Forces Medical Library announces the publication in May of a "Bibliography of Medical Reviews". The bibliography, arranged by subject, will contain approximately 800 references to review articles in clinical and experimental medicine and allied fields which have appeared in the calendar year 1955. Copies of the "Bibliography of Medical Reviews" will be available upon request to the Director, Armed Forces Medical Library, 7th Street and Independence Avenue, Southwest, Washington 25, D.C., United States of America, in the order of receipt.

LEONARDO DA VINCI.

OVER the last four centuries Leonardo da Vinci was universally recognized as one of the greatest artists of all time; and it was well known that he had founded his remarkable technique on a sound knowledge of anatomy gained from his own methodical dissections of the human cadaver. However, it is only in recent times that medical historians have become fully aware of the unique position occupied by this outstanding genius of the Italian Renaissance as a scientist, anatomist and physiologist. In actual fact, he was the initiator of entirely new trends in anatomical illustration and description towards the end of the fifteenth century. To achieve his purpose he decided upon a difficult and dangerous course—to disregard the dictates of ancient authority and investigate all nature with an open, free and observant mind. His life was reviewed in these columns on the occasion of the celebration of the fifth centenary of his birth in April, 1952.

In a small book of less than seventy pages by Elmer Belt we have an authoritative, illuminating and interesting account of Leonardo's epoch-making discoveries on many aspects of human and comparative anatomy.[1] The material presented was embodied in the fourth series of Logan Clendening Lectures on the History and Philosophy of Medicine delivered by Belt, who is professor of urological surgery at the University of California Medical School. Belt, who has been an acknowledged student of his subject for many years, first discusses Leonardo's innovations and discoveries in anatomy, giving a thorough outline of the extensive meanderings of his priceless manuscripts and anatomical drawings while they were in the precarious process of being handed down to an increasingly appreciative posterity. The concluding section of the book deals fully with the artist's comprehensive studies of the genito-urinary system.

The text is freely illustrated with reproductions of Leonardo's notebook drawings from the Windsor Castle Library collection and from a few continental sources. The study of these drawings would be enough in itself to convince the reader that Leonardo da Vinci was indeed an enlightened philosopher who used his rare gifts and unbounded energy in order to explore and interpret the universe by way of direct observation and experiment. It is certain that he was the first to represent the human body in true perspective for the guidance of the great anatomists who were soon to follow in his footsteps.

[1] "Leonardo the Anatomist: Logan Clendening Lectures on the History and Philosophy of Medicine", by Elmer Belt, M.D.; Fourth Series; 1955. Kansas: University of Kansas Press, Lawrence. 8½" x 5½", pp. 82, with many illustrations. Price: $2.00.

NORTH QUEENSLAND MEDICAL CONFERENCE.

THE North Queensland Medical Conference, which was held at Townsville last year, was a success in every way. Most of those who attended came from North Queensland, but many came from the southern part of the State and some from other States. The holding of medical conferences in North Queensland is seen as evidence of the virility of the local medical associations in that area, of the keenness of their members and of the desire to extend their knowledge. This year Cairns has been chosen as the venue and the date is June 25 to 30. This time the members of the Cairns Local Medical Association are acting as hosts and Dr. C. H. Knott is to be president. The provisional programme is interesting.

The conference will be opened by Alderman W. J. Fulton, Mayor of Cairns, and the inaugural address will be given by Dr. Otto Hirschfeld, Chancellor of the University of Queensland. Academic dress will be worn at the opening meeting. The programme has been grouped under the following headings: medicine, surgery, gynæcology and obstetrics, orthopædics, dermatology, pædiatrics, infectious diseases and "unclassified". Dr. R. B. Charlton and Dr. F. W. R. Lukin will be present as lecturers under the Queensland University Medical Education Scheme. A Trade Exhibition has been planned and social events for the week have been arranged. So far 76 medical practitioners have arranged to go to Cairns; of these 15 are from the southern part of Queensland and 17 are from other States. The conference membership fee is six guineas, and the honorary secretary is Dr. W. R. Horsfall, of the Commonwealth Health Laboratory, Cairns (Post Office Box 672). The climate in North Queensland in winter is proverbially pleasant and the hospitality of the people is more than generous. Members of the Association who are interested in a refresher course in the most agreeable surroundings imaginable are advised to write to Dr. Horsfall.

THE AUSTRALIAN RED CROSS SOCIETY.

THE members of the medical profession scarcely need to be told the virtues and practical worth of the Australian Red Cross Society. Its Blood Transfusion Service, now established throughout Australia and functioning with admirable technical and administrative efficiency, has become an indispensable and priceless handmaid of medical practice. Less spectacular but equally esteemed by thoughtful doctors is the research in hæmatology being carried out in many of the Service's centres. The many other activities of the Australian Red Cross Society, which are especially concerned with the needs of serviceman and ex-servicemen and which make a strong appeal to the general public, are met with from time to time in the course of medical practice; as citizens with a rare opportunity to appreciate the community's needs, doctors esteem these activities. Because the Australian Red Cross Society is a voluntary body, receiving government subsidy only for certain specific purposes, its wide service can continue only with generous support from the Australian people. Medical practitioners have more reason than most to understand why the Society's budget should be sufficient to cover the year's programme. They are therefore urged to give generous support to the Society's annual appeal being made this month.

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Abstracts from Medical Literature.

DERMATOLOGY.

Mepacrine and Chloroquine in the Treatment of Rosacea.

H. BRODTHAGEN (*Brit. J. Dermat.*, December, 1955) reports that as mepacrine and chloroquine have proved to be effective in the treatment of *lupus erythematosus*, it is reasonable to suppose that they would be equally effective in the treatment of other diseases, wholly or partly provoked by light. Accordingly a trial was made of the effects of these drugs in the treatment of rosacea. The series included 57 patients of all ages and with all stages of the disease. As criteria of the effects of treatment the author counted subsidence of infiltrations, pustules and diffuse redness as well as diminished subjective sensations in the lesion. Of the patients, 21 received mepacrine and 36 were treated with chloroquine. Some of the treatments were repeated. The dosage was two tablets daily during the first ten days and then one tablet daily for a minimum of three weeks. The mepacrine tablet contained 100 milligrammes and the chloroquine tablet 200 milligrammes. Side effects occurred mostly in patients receiving mepacrine, 19 patients developed yellow discoloration of the skin, and two seborrhœic dermatitis. With chloroquine, nine patients developed mild dyspeptic symptoms. One patient developed urticaria. No blood changes were detected. Of the 57 patients, 18 became symptom-free; of these 18 patients, 16 belonged to a group of 23, who had previously observed that the lesions were provoked by sunlight. The effects were most apparent during periods of long sunlight and high ultra-violet light intensity.

Sporotrichosis.

A. CARRIÓN AND M. SILVA (*Arch. Dermat.*, December, 1955) call attention to the rising significance of fungous infections in man, to the importance of mycological diagnosis in such infections, to the confusing problems of classification and to the need of further investigations towards the development of more complete definitions for the fungous parasites. They present a morphological study of a pathogenic species which produces subcutaneous nodular lesions resembling those of sporotrichosis in human beings, and which was originally described as a *Sporotrichum*, namely, *S. gougerotii*. According to the authors' observations, this fungus possesses several morphological characters which must be added to the original description of the species and which preclude its classification as a *Sporotrichum*. In the infected tissues the fungus appears in abundance as large, spherical, pigmented, coarse-walled cells, which multiply by internal septation followed by cleavage, and it is also represented by branched moniliform filaments which are produced by a series of successive buddings and which are reminiscent of *Cladosporium* sporulation. On artificial culture in the laboratory, it produces an invariably dark aerial and submerged mycelium, early growth in some media having a moist, yeast-like appearance. Microscopically its morphological appearances correspond closely with those of the so-called black yeasts. It possesses a yeast-like phase; it shows sporulating activities of the type of *Pullularia* and *Cladosporium*, and it is specifically characterized by the production of phialides which bear spores by abstriction at the apex and which are devoid of terminal receptacles of any kind. On the basis of these morphological characters the authors discuss the apparent affinities of the fungus with different form genera and recommend its assignment to the genus *Cladosporium* (*Hormodendrum*) until actual relationships among the dermatiaceous pathogens become better known.

Therapeutic Dyes and Cosmetic Effect.

H. EPHRAIM (*Brit. J. Dermat.*, December, 1955) discusses the rendering of the therapeutically effective dyes cosmetically acceptable. The dyes are mostly of the acridine or rosaniline variety, and the latter include gentian and methyl violet, brilliant green and basic fuchsin. The dyes are bacteriostatic and fungicidal. Gentian violet is also anti-inflammatory and a promoter of epithelialization. The healing action of dyes in the treatment of burns is due mainly to their valuable property of penetrating dead tissue and thus counteracting the danger of infection. A further property is the anti-pruritic action. The dyes are thus very useful agents, but their one great disadvantage is the disfiguring effect. To overcome this difficulty, the author had used the principle of colour mixing so as to obtain a shade as similar as possible to the colour of skin. This is satisfactorily achieved by mixtures of gentian violet, brilliant green, basic fuchsin and acriflavin in combination with a white powder. The author gives two examples of the prescriptions of such mixtures. He suggests that these make possible the unrestricted use of dyes in cosmetic-therapeutic preparations for any indicated use in uncovered parts of the body.

Prednisolone in the Treatment of Dermatoses.

L. FRANK AND C. STRITZLER (*Arch. Dermat.*, December, 1955) state that the topical administration of prednisolone in concentrations of 0·25% and 0·5% has some therapeutic effect on those dermatoses which respond to topically administered hydrocortisone, but is less effective than a 1% hydrocortisone ointment. Increasing the concentration of prednisolone from 0·25% to 0·5% does not increase its therapeutic effectiveness. Out of 256 patients, nine found prednisolone ointment irritating. The effect is probably that of a primary irritant on inflamed skin. Given systemically, prednisolone is an active and potent corticosteroid. The dermatological spectrum of conditions responsive to prednisolone seems to be very similar to that for hydrocortisone, and milligramme for milligramme prednisolone is about four times as effective as hydrocortisone. In therapeutic doses, prednisolone does not produce sodium and fluid retention or potassium depletion. An outstanding clinical feature is that patients can be treated with prednisolone without restriction of diet, and hypertension and sodium and fluid retention are not frequent complications.

Progressive Systemic Sclerosis.

W. N. PIPER AND E. B. HELWIG (*Arch. Dermat.*, December, 1955) state that generalized scleroderma involves the mesenchyme and may occur wherever connective tissue normally exists. The course of the disease is characterized by progressive involvement both in site and in degree of the skin and internal viscera, and this follows a generalized pattern. Involvement of the viscera may precede the appearance of cutaneous manifestations. The symptoms and clinical findings of scleroderma are, in general, not diagnostic, but are dependent upon the specific site and the degree of involvement. While circumscribed scleroderma has been considered to be a separate entity, a thorough search for other systemic involvement should be conducted on all patients with this cutaneous manifestation. Until the ætiology of generalized scleroderma has been established, "progressive systemic sclerosis", as proposed by Goetz, is suggested as a term more descriptive of the entity.

Trophic Skin Changes after Operations on the Trigeminal Nerve.

R. G. HOWELL (*Brit. J. Dermat.*, December, 1955) describes three cases of trophic changes in the skin following operations for the relief of trigeminal neuralgia. In each case there was crusting and scarring of the skin adjacent to the affected nostril, which was itself ulcerated and presented a punched-out appearance. In one long-standing case the alar cartilage was destroyed, with resultant severe disfigurement and contracted scarring extending into the upper lip. In two cases the trophic changes commenced within a few months of operation, but in one case the interval was three years. The crusts were easily removed, and underneath was a moist red surface tending to bleed easily. The condition is rare and is probably due to interruption in the sensory pathway of the fifth cranial nerve, though complete interruption is probably not necessary for the change. It is also possible that such trophic changes are related to undue picking and scratching of the affected skin, secondary to the sensory aberrations in the affected nostril. The author is of the opinion that treatment should be directed to local measures against secondary infection and to the avoidance of further trauma.

Cortisone in the Treatment of Pemphigus Vulgaris.

J. NEILL (*Brit. J. Dermat.*, December 1955) reports the response of a patient with *pemphigus vulgaris* to treatment with cortisone over a period of two years. Initially, the patient was treated with ACTH for a period of twenty-five days. Partial remission of the skin condition occurred, but the patient

developed a facial infection of bullous type with an antibiotic-resistant organism, which proved difficult to clear. The urinary ketosteroids were at subnormal levels before treatment, and no rise in the levels above normal figures occurred during treatment. The condition relapsed as soon as treatment was withdrawn. Cortisone treatment was commenced, and the patient was soon completely free of lesions on a daily dosage of 150 milligrammes. Attempts to replace the cortisone with ACTH were followed by local reaction and by relapse of the *pemphigus vulgaris*. ACTH was given in the belief that adrenal depression during cortisone therapy should be countered by periodic courses of the adrenal-stimulating hormone. However, the urinary ketosteroid levels rose very little during ACTH treatment, and the patient, for a short time, appeared to be resistant to cortisone. The patient was eventually stabilized on a dosage of 50 milligrammes daily. From this case the author deduces that ACTH is unreliable as the therapeutic agent. He states that the use of boosting doses of ACTH on a cortisone-depressed and damaged adrenal cortex may result in relapse of the original condition and in the precipitation of acute adrenal failure. He suggests that cortisone is the treatment of choice for *pemphigus vulgaris*.

UROLOGY.

Prognosis in Hypernephroma.

M. A. THROCKMORTON (*J. Urol.*, May, 1955) states that general argument has it that the outlook for patients with hypernephroma, considered statistically, is poor. Reported three-year survivals vary from 20% to 46%; five-year survivals from 11% to 46%; ten-year survivals from 6% to 22%. At the author's clinic 22 patients were reviewed for more than five years. Any immediate post-operative deaths were excluded from the survey. Of the 22 patients, eight were alive after five years. The ten-year survival rate is based on 14 cases, excluding post-operative deaths; two of the patients are alive.

Unilateral Renal Purpura.

J. ZELLERMAYER AND H. PASSMAN (*J. Urol.*, August, 1955), report a case of unilateral renal purpura with the characteristic pathological findings suggestive of hypersensitivity. The most significant of these was a marked eosinophile cell infiltration of the renal pelvic wall and of the peripelvic tissues. Nine similar cases have been reported in the literature. This is the tenth case to be reported. Many terms have been used to designate unilateral renal bleeding that has remained undiagnosed. It is now generally agreed that all bleeding kidneys will show some sort of lesion if they are adequately reexamined. In the authors' single case, every effort was made to exclude the well-known causes of hæmaturia. Furthermore, consideration was given to the possibility of the existence of rarer lesions such as hæmorrhagic papillitis, necrotizing papillitis, hæmangioma and other similar lesions. The finding of marked eosinophilic infiltration also described in the nine cases in the literature has led to the conjecture that a sensitivity factor could be responsible; yet in no instance was such a factor found. The gross study of these findings revealed slightly dilated calyces and renal pelvis with petechiæ in the pelvic mucosa. The ureters were found to have petechiæ in several of the cases as well as in that of the authors. Microscopic examination revealed the presence of subepithelial pelvic hæmorrhages, dilated blood vessels and inflammatory infiltration with large numbers of eosinophile cells. Various theories have been adduced as to the possible cause, such as circulating injurious agents, infection, congenital weakness of vessel walls, metabolic factors, and hypersensitivity. In the authors' case there were gross hæmaturia and pain from thrombic obstruction. Persistence of a filling defect, which was really due to blood clot, led to the diagnosis of neoplasm, and thence to the performance of nephrectomy.

Malignant Tumours of Renal Parenchyma.

R. K. ROYCE AND A. R. TORMEY (*J. Urol.*, July, 1955) have made a review of 102 cases of malignant renal parenchymal tumours in adults. None occurring later than 1949 was included so as to afford an adequate period for the follow-up. The patients were 82 males and 20 females. Tumours in children (mostly the Wilms type) and pelvic epithelial tumours are not included in this study. The average age was about fifty-six years, and the ages ranged from twenty-four to eighty-two years. In this series, 11 patients received no treatment; some of these were admitted to hospital *in extremis*, in the other cases death was due to another disease and the correct diagnosis was made at autopsy. There were 75 nephrectomies, with 11 post operative deaths. There were 22% of five-year survivals, and 18% of patients survived for longer periods than this. The histologically well-differentiated growths had a far better prognosis than the poorly differentiated ones. Smaller tumours had a better prognosis than larger ones. There was no relation between the pre-operative duration of symptoms and the prognosis. The age of the patient was not related to the prognosis. The presence of dilated perirenal veins was usually associated with an inoperable tumour. Post-operative mortality prior to 1943 was 18% (in 55 patients) compared to only 2% after that year (47 patients). Of the 102 patients of the whole series, 81 died during the period of study; the remaining 21 patients are either still alive or untraced. Of the deaths, 66 were due, apparently, to carcinomatosis; 13 of these were confirmed by autopsy. The other 53 patients were known to have had recurrences, but died either at home or in some other hospital. Of the 11 post-operative deaths, six were due to shock and hæmorrhage. One patient died of atelectasis and secondary pneumonia, one died of aspiration pneumonia, one died of anterior (transperitoneal) wound disruption. Two patients died of sepsis from associated lesions in the kidney (pyonephrosis and perinephric abscess) and in neither of these subjects was removal of the kidney possible. For 16 patients with radiologically demonstrable pulmonary metastases and in two with metastases elsewhere, the average survival time was only seven months. Twenty-seven patients were found to have local extension of growth outside the kidney; their average survival time was 5·7 months. For ten patients who were found to have local extension as well as venous invasion, the average survival was 7·1 months. Two patients, who had gross tumour thrombi in the renal vein alone, survived for four and ten months respectively. Two other patients had neoplastic invasion limited to the small intrarenal veins near the growth, and they have survived for five and twelve years respectively and are free of recurrence. They did not receive X-ray therapy. The authors have not noticed any improvement in survival results from the use of ordinary X-ray therapy. Supervoltage X-radiation has not been used.

Aluminium Gel Dietary Prophylaxis after Extensive Nephrolithotomy.

R. M. SPELLMAN AND V. F. MARSHALL (*J. Urol.*, April, 1955) allege that the high incidence of the recurrence of calculi after very extensive nephrolithotomy, as for the removal of staghorn calculi, is well known. The rate varies, according to different authorities, between 45% and 75%. The results in 18 cases of typical staghorn calculi have been reviewed. Fourteen of these cases were reviewed for growth or recurrence of stone for periods of from one to seven years after operation. In no instance did either a new stone appear or a residual fragment grow larger, while the patient was definitely following the post-operative programme of treatment. In some instances defection from the prophylactic regime soon resulted in a recurrence.

Acceleration of Excretion Urograms by Ingested Ice Water.

S. A. KAUFMAN (*J. Urol.*, August, 1955) states that it was noticed recently (1952) by Herzan and O'Brien that ureteric colic was relieved and that the delayed excretion of opaque medium was hastened by the ingestion of iced water. The authors had the opportunity of observing and of confirming this phenomenon in a man aged forty-five years, and they consider that this simple method is deserving of wider promulgation. The cause of the pain in patients with renal calculus may be ureteric spasm; it is well known that any form of blockage may be accompanied by temporary failure of the kidney to excrete contrast media. In the author's case no excretion was seen on the left side for up to sixty minutes after administration of the opaque medium, but a clear nephrogram had been developed, and the patient's pain was still present. He was given a glass of iced water; there was almost immediate relief of pain, and an exposure made just after this showed contrast medium in the calyces, pelvis and ureter, with no sign of obstruction. The mechanism through which this effect is achieved is not understood, though it is probably reflex in origin and not the result of diuresis.

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British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on October 29, 1955, at the Wagga Wagga Base Hospital, Wagga Wagga, DR. H. H. WILLIS, the President, in the chair.

The Arthritic Diseases and their Treatment.

DR. SELWYN NELSON read a paper entitled "The Arthritic Diseases and their Treatment" (see page 521).

Hand Injuries.

DR. P. H. GREENWELL read a paper on "Surgery of Hand Trauma" (see page 526).

DR. H. H. WILLIS asked Dr. Nelson why he classified ankylosing spondylitis as a separate disease from rheumatoid arthritis; most text-books considered them as the same. Dr. Willis also asked Dr. Nelson whether he could state the cause of ankylosing spondylitis; he had already said that he did not know the cause of rheumatoid arthritis. That was refreshing, seeing that the text-books gave so many causes for it—which was the origin of many abuses of the medical benefits under the National Health Scheme. Dr. Willis then asked Dr. Nelson to defend his statement that patients suffering from rheumatoid arthritis should be admitted to hospital. Dr. Nelson had shown a picture of a magnificent institution in the United States of America where a whole floor was devoted to the care in bed of patients of that sort. In Australia hospital beds were few, and as the population increased the scarcity of beds was likely to increase, for the next ten years at any rate; it was therefore the opinion of some that there should be devised means of treatment in the home rather than in hospital. Dr. Willis asked Dr. Nelson whether it was really necessary that patients suffering from rheumatoid arthritis should be admitted to hospital.

Dr. Nelson, in reply, said that he was prepared to defend his reasons for putting ankylosing spondylitis and rheumatoid arthritis in two separate categories. In the first place, rheumatoid arthritis attacked first the peripheral joints and ankylosing spondylitis attacked first the sacro-iliac joints and the apophyseal joints of the spine. Secondly, X-ray therapy had no effect on rheumatoid arthritis, but it had quite a large effect on ankylosing spondylitis. Thirdly, for what it was worth, gold therapy had no effect on ankylosing spondylitis, but it had a definite effect in a number of cases of rheumatoid arthritis. Dr. Nelson went on to say that the main origin of the identification of the two diseases was in America. When he was in that country in 1954, he had tackled various rheumatologists on that subject, and when they were spoken to singly, they all agreed that the two diseases were separate, although collectively the opposite statement was still made in the text-books, and in the American classification of the rheumatoid diseases, ankylosing spondylitis appeared as rheumatoid spondylitis. Dr. Nelson said that Professor Kellgren, who was the only professor of rheumatic diseases in an English-speaking university, had various theories about the causes of ankylosing spondylitis. He considered that there were several varieties of ankylosing spondylitis, some of which were associated with Reiter's syndrome (urethritis *et cetera*), and he thought that in Europe that form of ankylosing spondylitis was common. In other cases the ætiology was not related to that type of infection, and there were various theories about it. Dr. Nelson said that in his opinion there was one thing that rheumatoid arthritis and ankylosing spondylitis did share, and that was an unknown ætiology. In reply to Dr. Willis's question about the necessity for treating rheumatoid arthritis patients in hospital, Dr. Nelson said that in the clinic at the Royal Prince Alfred Hospital they probably recommended for admission about 3% of the total rheumatoid population under their care; in other words, 97% were treated as out-patients. Dr. Nelson said that the statements in his paper were to the effect that the majority of cases of rheumatoid arthritis were mild, that the very severe cases required the patient's admission to hospital, and that some cases were so severe that no ambulatory treatment was possible, mainly because of involvement of joints that prevented the patients from walking, and they were very sick people. Such patients demanded and should be granted admission to hospital. Opinion overseas was that many of the more mildly affected patients would do better if they were admitted to a special ward, where they had not so much the hospital atmosphere as a combined rehabilitation-boarding house atmosphere, and where they could have some rest and some exercise and other forms of treatment. They would thus be saved the problem of battling with public transport to go to hospital. One of the difficulties at the arthritis clinic experienced in treating some patients adequately by physical measures was that they were exhausted by the battle to get to the physiotherapy department for treatment. One had to compromise, and perhaps give them short of ideal treatment. Dr. Nelson thought that, although they recommended for admission to hospital only 3% of the patients, if they had more facilities they would send more for admission on that basis.

DR. J. F. ZIEGLER asked Dr. Nelson to comment on one line of treatment if only to condemn it—the bone-boring of the metaphysis. Dr. Ziegler said that about fifteen years earlier the senior surgeon at a large city hospital apparently noticed that if a fracture occurred in a limb, the contiguous joints, if affected by rheumatoid arthritis, lost their arthritis. On that basis he developed a system whereby he used to bone-bore the metaphysis in the region of the joint. Admittedly, when the joint involved was one with multiple bones, such as the wrist joint, the relief of pain might have been attributable to ankylosis; but in the case of a knee that was not so. Over a period of two years Dr. Ziegler was in a corresponding out-patient clinic; in that two years, he thought that at least one patient per day came in to have other joints in the body treated, contending that he had experienced complete relief of pain in the joints that had already been bored. Dr. Ziegler said that the surgeon in question was treated as a crank, and the only basis for the treatment was what had been already given. At a later stage, the surgeon said: "The joint has been insulting, I'll insult it back"; that was obviously not a very logical statement. The surgeon used to contend that the fluid exuded was pale. Dr. Ziegler thought that whilst one could hardly make the comparison in ordinary tissues, the exuded fluid did seem paler than would have been expected from ordinary bone marrow. Dr. Ziegler asked for Dr. Nelson's opinion on the matter.

Dr. Nelson, in reply to Dr. Ziegler, said that he thought the method should be added to the list of new and non-official remedies. He had no personal knowledge of that method of treatment, and was interested to hear that it was advised. He could offer only one possible explanation for the improvement, apart from the psychological one; that was that the insult was not so much to the region as to the patient's pituitary adrenal cortical axis, with a slight increase in the outflow of steroid. To give a proper comment, one would have to know whether the disease was active or not and various other things about it. Dr. Nelson said that it reminded him of stories told about the south coast in earlier years. From time to time whales used to be washed up on the beach. One young man was persuaded that if he went inside a whale at a suitable time, his rheumatism would be made better. It was not known whether the effect on his rheumatism was as expected; but at least he was socially ostracized for some time.

DR. H. W. AUSTIN asked Dr. Nelson to comment on the value or otherwise, firstly of the local use of procaine lactic acid, and secondly of the systemic use of "Atebrin".

Dr. Nelson, in reply to Dr. Austin, said that the local use of procaine lactic acid had been introduced by Waugh, of Liverpool, and Dr. Nelson had seen him carrying it out in 1947. It was mainly for osteoarthritic joints. Dr. Waugh had taught him a number of new ways in which to enter various joints. The theory was that the synovial fluid of osteoarthritic joints had a slightly different pH, and that the use of lactic acid tended to correct it. Dr. Nelson said that he had actually used the treatment, and particularly in the case of the hip he thought it produced beneficial results. The treatment had really been superseded by the use of hydrocortisone, which was not available at that time. Referring to the systemic use of "Atebrin", Dr. Nelson said that that treatment had been first published some years earlier by Francis Park, of London, the drug being "Mepacrine". L. J. A. Parr, of Sydney, had read a paper on the subject at the Ninth Session of the Australasian Medical Congress (British Medical Association) held in Sydney in August, 1955; he had reported a few favourable results from the use of "Mepacrine". The main disadvantage was that his patients' skins turned yellow. Dr. Nelson said that he himself had not used the treatment.

DR. J. L. TUNLEY asked Dr. Nelson to comment on the value of PAS given systemically.

Dr. Nelson, in reply to Dr. Tunley, said that a certain number of patients showed a favourable response, which

seemed to him to be comparable with the favourable response obtained by the administration of salicylates. It was not possible to measure the salicylate levels in the blood of patients on PAS therapy; whatever happened to the PAS, it did not appear in the blood as salicylate. Nevertheless, the type of response appeared to be similar to, but not as good as, that obtained by salicylate therapy. Dr. Nelson thought that the general consensus of opinion at the present time was that PAS given systemically was not a valuable aid in the treatment of arthritis, and that it was better to use salicylates.

DR. L. E. GOLDSMITH asked Dr. Nelson how important he considered the blood sedimentation rate in the diagnosis and as an indication of progress. Dr. Goldsmith then referred to cases of acute rheumatoid arthritis which was very painful, and in which one might consider the administration of gold. He asked Dr. Nelson whether the dangers of combined "Butazolidin" and gold would be too great.

Dr. Nelson, in reply to Dr. Goldsmith, said that it was not possible altogether to get a mathematical correlation between the erythrocyte sedimentation rate and the severity of the disease, although they often did correspond fairly closely. As far as the response to treatment was concerned, he thought that the erythrocyte sedimentation rate did parallel fairly closely the developing remission of the disease. The exception to that was that when "Butazolidin" was given as a solitary therapeutic procedure, there was more clinical remission than appeared by estimation of the erythrocyte sedimentation rate. Discussing the concurrent use of gold and "Butazolidin", Dr. Nelson said that both were marrow-toxic drugs, but they could be used together if one was prepared to take more stringent precautions in white cell counts than one would normally take. Dr. Nelson said that he had used "Butazolidin" after gold and gold after "Butazolidin", but he preferred to use them together. If the extra precaution was taken, it was justifiable. They had slightly different actions, one being a suppressive and the other an analgesic.

DR. R. H. KENNY asked Dr. Nelson whether in his experience he had noted any specific X-ray changes in the lungs of patients with rheumatoid arthritis. The question had been raised in the *British Medical Journal* about seven or eight months earlier. In a survey of Welsh miners they had found specific changes—something in the nature of a miliary infiltration; but Welsh miners also developed progressive massive fibrosis which was more or less specific to them. Recently there had been another article in the *British Medical Journal*, reporting that no specific changes had been found in the general population. Dr. Kenny asked for Dr. Nelson's comments.

Dr. Nelson, in reply to Dr. Kenny, said that in so far as he had investigated that problem they had found no specific changes. The Welsh Miners' Research Unit and Professor Kellgren's Rheumatism Research Unit had worked in very close cooperation and utilized the same field workers for the survey of the prevalence of rheumatoid arthritis and other forms of rheumatic disease. Dr. Nelson agreed with Dr. Kenny that the changes found might have been due to the fact that the subjects were miners. He did not think that there was any real evidence that there was a higher incidence of rheumatoid arthritis amongst them than amongst the general community. Dr. Nelson said that there was another way in which lung changes might occur in a patient with rheumatoid arthritis; such a patient might have primarily a lung disease, such as bronchogenic carcinoma, and it might be months or even years before the diagnosis of bronchogenic carcinoma was established. The patient might have been suffering from arthritic changes which were difficult to distinguish from rheumatoid arthritis. One had to be on guard with patients who had some chest condition, to be sure that one was not dealing primarily with a case of lung carcinoma masquerading as rheumatoid arthritis.

DR. G. L. HOWE asked Dr. Nelson about his patients with ankylosed hip joints. Dr. Howe said that Dr. Nelson knew, and he himself knew through his association with the Home for Incurables, that a great number of people became bedridden because they had ankylosed hip joints. It was extremely difficult to have cup arthroplasties performed. The time during which a hospital bed was required was the biggest factor. Dr. Howe wondered whether experience of a large number of cases showed the results to be good, and what criteria were necessary in the selection of patients for operation.

Dr. Nelson, in reply to Dr. Howe, said that first of all the patient should be reasonably fit; it was no use operating on a frail old person. The post-operative care was the essential part of the job. The patient needed to have grit and determination and must be able to carry out the post-operative exercises if a good result was to be achieved. The first requisite in the selection of patients for operation was to exclude all those who were not likely to qualify in that way, and then one should consider those who remained. They would fall into two groups: (i) those whose condition could be controlled by medical measures to a stage of reasonable comfort; (ii) those whose condition could not be so controlled. Those in the second group needed the operation. Dr. Nelson agreed that it was difficult to get a bed for them. The general consensus of opinion was that the use of the cup arthroplasty was superior to the acrylic head, because it had a longer duration. The patients he had seen who had had the operation had been overjoyed with the result; they had about 75% range of movement restored and they had a painless joint. Uniformly good results would be obtained only if the patients were carefully selected first. Some form of arthrodesis would be better for other patients. Abduction-flexion deformity could be corrected and made painless and stable by arthrodesis.

DR. S. P. TRENERRY first asked Dr. Nelson whether cortisone was being given to out-patients at the Royal Prince Alfred Hospital. He next asked whether there was any point in giving ACTH at the end of a course of cortisone. Dr. Trennery finally asked whether the sulphonamide drugs were now used in treatment.

Dr. Nelson, in reply to Dr. Trenerry, said that the answers to the first two questions were in the affirmative. In reply to the third question, Dr. Nelson said that he had no personal experience of the use of sulphonamide drugs. He had seen some patients with toxic reactions from sulphonamide treatment; he did not think it offered the benefits of some of the other forms of treatment, and yet it carried with it an appreciable risk of trouble. Other workers had reported favourable results.

DR. R. W. ACKLAND had a problem for Dr. Nelson. He said that he had a patient with rheumatoid arthritis who was bed-ridden, but could be got out into a wheel-chair. She had a rare condition of the eye, *scleromalacia perforans*. The ophthalmologists wanted her to go to Sydney for treatment; she thought that the journey would be too much for her. Dr. Ackland asked Dr. Nelson whether she could be treated for the rheumatoid arthritis and whether that would improve the condition of her eyes; she was gradually losing all the sclera and there were choroid changes.

Dr. Nelson, in reply to Dr. Ackland, said that there were several ways in which rheumatoid arthritics developed changes in the eyes. Sjögren's syndrome, in which the eyes were dry, might occur. Even in ordinary rheumatoid arthritis sometimes chronic episcleritis occurred, or some other disorder of the collagen tissue of the eye. In Reiter's syndrome there was coexisting conjunctivitis, urethritis *et cetera*. Dr. Nelson presumed that in Dr. Ackland's patient the arthritis was still active, and that the erythrocyte sedimentation rate was still raised. He asked Dr. Ackland whether the eye people had suggested either the local or the systemic use of cortisone.

Dr. Ackland said that cortisone had been used locally on the eyes.

Dr. Nelson said that there were very few patients with rheumatoid arthritis who were so ill that they could not be moved; but before the patient undertook the journey to Sydney, it would be necessary to be sure that she was going to get some benefit to her eye condition.

Dr. Willis said that an eminent surgeon of a previous generation had said that the principles of surgery never changed. From Dr. Greenwell's paper he had gathered that they did change; he had heard some things that were different from what he had been taught. Dr. Willis then called upon Dr. T. Y. Nelson to open the discussion.

DR. T. Y. NELSON said that there were very few who had a great deal of experience in the branch of surgery under discussion. That was one of the most important lessons to be learnt from Dr. Greenwell's paper. There was no doubt that one of the biggest problems of any public hospital was the organization of its staff; that, in his opinion, was where the greatest advances in hand surgery and other difficult types of case could be achieved. Dr. Greenwell had shown other hospitals what could be accomplished in hand surgery. Dr. Nelson said that in his early days that type of surgery used to be relegated to the junior resident medical officer; it was the first thing that the house doctor did when he went to the casualty room, and the results were appalling. Dr. Nelson went on to say that it mostly used to be taught that no tendon graft was successful in the palm. Tendon grafts on the dorsum of the hand were much easier. There were many reasons why it was possible to get good results

in those difficult cases. The first was organization, which involved the drafting of such cases into particular groups, so that they were handled by one, or at most two, pairs of hands. There were special instruments. Above all, as Dr. Greenwell had said, there was time. Dr. Nelson said that he thoroughly agreed with Dr. Greenwell that one of the most important things to be aimed at was thorough cleansing before any form of surgery was attempted. Dr. Nelson asked Dr. Greenwell one question: in the treatment of tendon injuries in that difficult no man's land, how long did he delay before performing the tendon graft? Dr. Greenwell had mentioned six months in a case that he had discussed. Dr. Nelson wondered whether that was his usual practice, or whether in other cases he performed the graft earlier.

Dr. Greenwell, in reply, said that Dr. Nelson's early experience had been no different from his; that was one of the reasons why he had tried to do something about the position. In reply to Dr. Nelson's question, Dr. Greenwell said that six months was not a common period of delay before grafting. In the specific case mentioned the boy was young, which in part determined the delay; and provision had been made for keeping the finger mobile by physiotherapy. That was uneconomic in most cases. Usually the operation was performed four to six weeks after primary healing had occurred. In all cases a period of approximately two or three weeks was allowed between complete healing and tendon graft, as the advent of infection in the presence of a graft was disastrous.

DR. K. R. HEBER asked Dr. Greenwell what his views were on digital and wrist block as far as gangrene was concerned.

Dr. Greenwell, in reply, said that there had been certain cases, he thought mostly continental, in which gangrene had followed on blocking, particularly in the finger. In those cases, he thought that without exception a tourniquet was used. In this technique, a tourniquet was placed around the finger tightly, and a ring injection was given distal to the tourniquet. It was a very effective anæsthetic, because the anæsthetic agent was held in the area and one had the advantage of a tourniquet. But the danger of gangrene was present, and the method was not used in his clinic. It was interesting to note that in these cases local anæsthetic with adrenaline had been used. At his clinic in giving block injections they did not employ adrenaline at all. The anæsthetic agent which they were using at present, and which was very satisfactory, was "Xylocaine"—a common agent in dental anæsthesia. Dr. Greenwell thought that when it was used without adrenaline and in the absence of tourniquet control, there was no danger. At Sydney Hospital blocking of the digital nerves in the metacarpal region or wrist block was used.

DR. A. S. JOHNSON said that he agreed entirely with what Dr. Greenwell had said; his paper had embodied all the modern principles in hand surgery. Dr. Johnson said that a few years previously, in the course of his duties in urgent surgery at the Royal Prince Alfred Hospital, he had had to deal with quite a number of hand injuries. Dr. Johnson joined with Dr. Greenwell and Dr. Nelson in stressing the great importance of adequate cleansing of the hand; the people who had been engaged in the cleansing process should, if they were connected with the operation, change their gloves and gowns before proceeding with it. Referring to tendon suture, Dr. Johnson said that the general policy at the Royal Prince Alfred Hospital was along the lines suggested by Dr. Greenwell; extensor tendons were dealt with by primary suture, and flexor tendons, in the no man's land referred to, by some delayed method. Dr. Johnson asked Dr. Greenwell what he thought about the secondary suture of a flexor tendon in that region rather than a grafting operation. By that he meant the secondary suture of the *flexor profundus* alone with removal of the *sublimis*. It was agreed that either primary or secondary suture of both flexor tendons in that no man's land was useless; but perhaps sometimes when the wound was clean and the tendons were lying in apposition, even in a delayed case, consideration might be given to the question of removing the *flexor sublimis in toto* and suturing the *flexor profundus*. At the Royal Prince Alfred Hospital there was no clinic like Dr. Greenwell's clinic at Sydney Hospital. At the same time, for many years it had not been the custom to have even lesser hand injuries attended to by junior resident medical officers. All patients with hand injuries, even relatively minor injuries, were admitted to hospital and dealt with by the assistant surgeon concerned.

Dr. Greenwell, in reply to Dr. Johnson's question, said that he could only plead inexperience. He had on only two occasions employed the method mentioned. He was not satisfied with the result in either case, and since that time he had almost exclusively used the *sublimis* grafting operation. He thought that in most clinics where the problem was commonly encountered, the tendency was towards the use of grafting operations. American surgeons tended to employ the *sublimis graft*, while in most English clinics more commonly the *palmaris longus* graft was used. Insurance companies, which were a fair index of the success or failure of an operation, at the present time were in favour of the grafting operation in most cases.

DR. P. T. MILLARD asked for three points to be made clearer. He referred first to Dr. Greenwell's cases in which a finger required repulping and a cross-arm graft was used. Dr. Greenwell had spoken of preserving the nail matrix and subsequently treating the graft and allowing the nail to grow again. Dr. Millard wanted to hear more of what was done. With regard to the relative merits of a cross-arm graft and an abdominal flap, Dr. Millard said that it seemed that there was nothing more disabling than a cross-arm flap; the patient was handcuffed and could do nothing for himself. He wondered whether the cross-arm flap was often employed. Finally, referring to the flexor tendon graft, Dr. Millard said that Dr. Greenwell had spoken of the *sublimis* tendon being attached to a prepared area on the distal phalanx. Dr. Millard wondered whether it would not be possible in most of those cases to use the existing tendon, and suture the graft to the distal fragment.

Dr. Greenwell, in reply to Dr. Millard's first question, said that they had in the case mentioned been fortunate enough to have the nail matrix retained. Dr. Greenwell said that he would not always act as he had done in that case; he certainly would not do so if the patient was a labouring man; but the patient in question was a girl, aged seventeen years, and cosmetic considerations led to the decision. If one was to employ the cross-arm flap or any sort of a pedicle flap to a finger-tip, the nail had to receive consideration. Perhaps in many cases it would be better to remove the retained portion of the nail and to accept the completely skinned finger. Referring to the problem of deciding whether to use a cross-arm or abdominal flap, Dr. Greenwell said that the difficulties were overcome if it was possible to use a cross-finger flap. He explained carefully to the patient what was involved. If an abdominal flap was used, the patient would be immobilized in bed, or if a cross-arm flap was used, the patient would be ambulatory, but would have to be assisted in all other ways. The patient in question had elected to have a cross-arm flap. It was important that the patient should understand what was contemplated: the picture should be clearly painted and the patient should assist in making the decision. It did not really matter which was used, but perhaps a better match was obtained cosmetically with arm skin than with abdominal skin. An area on the abdominal wall that was not hair bearing should be chosen. If a cross-arm flap was to be used, skin on the inner side of the arm must be employed. In reply to Dr. Millard's third question, about the tendon attachment, Dr. Greenwell said that he had at times attempted to attach the tendon to the terminal portion of the existing tendon attachment. It was generally agreed that to do so was not satisfactory. In one case he had dealt with two tendons, one by the method suggested, one by the generally accepted method; and he thought that the second was the better. He thought that most operators excoriated the base of the phalanx and attached the abraded tendon to it.

DR. G. L. HOWE referred to a common problem that had not been discussed—that of crush injuries causing fractures of the proximal and sometimes the middle phalanx with a considerable amount of abraded soft tissue and tendons lying loose in the wound, and yet the circulation was maintained. Dr. Howe asked Dr. Greenwell whether he was ever able to get a functional result in such cases.

Dr. Greenwell, in reply to Dr. Howe, said that if the finger was disrupted to the extent described, the problem was one of amputation. The principle of retaining at all costs could not always be applied. In the case described there was bony loss with considerable skin loss, and there would not be much chance of giving that finger mobility. Certainly a great deal of periarticular thickening and stiffness would be present.

Dr. Johnson spoke again. He asked Dr. Greenwell what was the policy in regard to the use of antibiotics in the treatment of hand injuries. Dr. Johnson wondered whether they were given as a routine, and whether sulphonamides and penicillin were used locally.

Dr. Greenwell, in reply, said that in his clinic antibiotics were employed as a routine procedure; usually penicillin was given in the form of procaine penicillin, 300,000 units, twice a day. Seldom were any other antibiotics used unless there were special indications. A penicillin "cover" was used for a period of approximately five days.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

A REBUKE AND A REPLY.

[From the *New South Wales Medical Gazette*, May, 1875.][1]

WE have been rebuked for publishing in our last issue certain articles considered indelicate and unsuited to the perusal of the gentler sex. To this we reply that we should be exceedingly sorry wantonly to shock modesty: but although we desire the Medical Gazette to circulate among those who are not of the medical profession we do not profess to deal in milk for babes. A medical journal must ex necessitate contain much not intended for the feminine eye and its proper place is the study and not the drawing room. We would remind those inclined to cavil that "to the pure all things are pure".

Correspondence.

THE BAN ON HEROIN.

SIR: For some years I have been perturbed about the consequences of restricting the import into Australia of diamorphine salts and heroin. Apparently these restrictions were imposed by the Commonwealth Government in order to comply with a request from the World Health Organization.

During the past nine months I have visited most countries in Europe and also Canada and the United States and was able to gain first-hand knowledge concerning the control of heroin, particularly in the United Kingdom and in Northern America. I was also privileged to attend the debate on this subject which took place in the House of Commons towards the end of last year.

The Government of Great Britain were frustrated in their efforts to ban the manufacture of heroin in that country only on legal grounds, but their actions aroused tremendous hostility from many members of the medical profession. Practically every physician with whom I spoke who was actually associated with the clinical administration of the drug was strongly in favour of retaining the right to prescribe it. The British Medical Association were against the ban, as also were the following leading hospitals in London: The London Hospital, Barts, Charing Cross, King's College, Saint Thomas's, The Royal Marsden (formerly Cancer Hospital), Hammersmith and The Brompton—surely a good cross-section of the teaching institutions.

There is very little known heroin addiction in England; yet in the United States of America, where the ban has been in operation since 1924, the number of addicts is estimated at anything from 100,000 to 1,000,000 persons, and already addiction to the phenobarbital group of drugs is presenting a problem. The ban on heroin certainly did nothing to relieve the position of addiction to that drug; and if the United States of America is to be consistent in its measures, the phenobarbital group of drugs should be banned also. Present-day physicians in America have had no clinical experience with heroin and are therefore in no position to evaluate its worth.

It appears that before heroin should be banned in this country one should ask: "Is there or is there not in all cases an adequate substitute for heroin?" I believe through personal experience that there is no adequate substitute for this drug in every case, particularly in advanced tuberculosis with intractable cough and in certain forms of malignancy, especially when one wished to give the patient a sense of euphoria. It was also stated in England that heroin was the only drug which could give relief to pain in cases of severe burns, and that if atomic weapons were used, we would want every ounce of the drug we could obtain.

Morphine, heroin, pethidine and phenobarbital are drugs known to give rise to addiction; why select one drug to ban? I agree with D. R. W. Cowan that we should not blindly accept the dictates of the World Health Organization experts who seek to impose a universal ban on this drug. It is well known that there is a difference of opinion amongst the medical profession of Australia concerning the use of heroin, and for this reason alone, I maintain that the Government has no right to legislate so that it cannot be prescribed.

Yours, etc.,
R. MUNRO FORD,
Medical Superintendent.

The Morris Hospital,
Northfield,
South Australia.
March 9, 1956.

[1] From the original in the Mitchell Library, Sydney.

CORONARY DISEASE AND MYOCARDIAL INFARCTION.

SIR: In your issue No. 7 (M. J. AUSTRALIA, February 18, 1956, page 294), under "Current Comment", is published an unsigned article titled "Coronary Disease and Myocardial Infarction". I assume that this bears subeditorial status. The article briefly compares and contrasts the findings in two other articles appearing in different journals, namely, that of Manchester workers, Snow, Morgan Jones and Daber (1955), and that of Boston workers, Blumgart, Schlesinger and Davis (1940). In so far as the British workers criticize the American, and in so far as your comment quotes and accepts this criticism as valid, I ask space in your columns to discuss the matter. The criticisms of Snow *et alii* have been given weight as well as promulgation by your subeditorial.

There is no doubt of the value of the Manchester work and of the importance of this type of morbid anatomical study in general. I personally regret that Snow *et alii* have to such an extent used their work to refute one aspect of the wide scope so remarkably covered by Blumgart *et alii*. Surely the major conclusion of Snow *et alii* from finding 59 infarcts in 25 hearts should have been that infarcts are as a rule multiple They do, I know, make this point, but in their discussion the main theme is to contradict what I shall show is a conclusion unjustifiably drawn from the American work.

However, I write to comment on the following quotations:

1. From Snow *et alii* (*loco citato*, page 507): "They (Blumgart et al.) claimed that occlusion of a main coronary artery occurred very frequently in man without any corresponding myocardial infarction. . . . This . . . has had a considerable influence upon the way in which both pathologists and clinicians have since thought about the sequence of events in the heart in coronary disease. It became easy for the pathologist to accept conspicuous coronary occlusion in the absence of demonstrable infarction, and when a prolonged attack of cardiac pain occurred without the associated changes of infarction in the electrocardiogram, the clinician was ready to attribute it to coronary occlusion without infarction."

2. From "Current Comment" in the journal (*loco citato*, page 294): "Many current text-books of cardiology and pathology quote and accept the important work of Blumgart . . . which . . . apparently demonstrated that occlusion of a coronary artery was frequently not followed by myocardial infarction."

Both Snow *et alii* and "Current Comment" go on to say that Blumgart and his colleagues reported that in 30 subjects 53 main vessel occlusions gave rise to only 16 infarcts.

Now it is fair to state quite strongly that nowhere do Blumgart *et alii* allude to such figures. Their article is a ninety-page affair, and despite many readings over the years these figures came as new knowledge to me. The figures have been culled (in a statistical sense perhaps justifiably) from the three main tables in the American work, as I myself have since culled them. Thus it would appear that Snow *et alii* have counted the number of abbreviations used for main vessel occlusion in the three tables of the original article (and they have not done it by studying the protocols, because the tables and the figures in the protocols do not exactly agree) and that they have counted the number of abbreviations used for infarction and in this way have arrived at these extraordinary figures—53 main occlusions and 16 infarcts. They have not alluded to the number of multiple occlusions in one vessel, the site of the occlusion, its nature, nor its apparent rate of formation. (I know that they have ignored these details in their own statistics.) Snow *et alii* have counted the 16 infarcts testified to by Blumgart *et alii* in their tables by the abbreviation "+" and

have ignored the four which Blumgart *et alii* listed as probable by the abbreviation "O*" (Blumgart's cases 4, 7, 22 and 24), and they have ignored the other two (Cases 1 and 2), which, if they had studied the protocols closely, they would have found to be at least likely. If they had analysed the 53 main vessel occlusions which they extracted from the tables, they would have found that 13 are in peripheral parts of main vessels, three are peripheral emboli from a more proximal thrombus in the same vessel, and two are terminal thrombi occurring the one (Case 11) in a patient with uncontrolled hæmatemesis and the other (Case 26) in a patient dying in congestive failure. In their first 12 cases Blumgart *et alii* were attempting to assess the state of the coronary circulation in patients with uncomplicated angina, and they tended to disregard to that end (and only to a limited extent) the final occlusive event with its infarct. It is not true to infer that the American workers failed to make a histological examination of the myocardium. I believe that it is fair criticism of the otherwise splendid work of Blumgart *et alii* to state they have erred in accepting too readily the absence of early necrosis, and in not accepting as infarcts what they describe as large areas of fibrosis which "would ordinarily be regarded as healed infarcts" (Blumgart *et alii, loco citato,* page 81). I think it fair without even taking this last fact into account, and for the reasons stated above, to change the extraction from these tables so that we conclude that the work of Blumgart *et alii* shows (this is different to saying that they reported) that 35 significant main vessel occlusions produced 22 infarcts, which is rather different to the figures 53 and 16. In your opening reference to the American work you do not use the important adjective "main" to qualify the noun "vessel".

Now Snow *et alii* have not at the time of writing published their protocols in detail. Judging from their October article (*loco citato*), we find that they have classed as separate infarcts superimposed and contiguous lesions, which, in their terms, could be regarded as areas of progressive necrosis. It is true that this is often found and that it is possible to recognize different infarcts as being superimposed on one another. However, one must take issue with them on their case No. 15, in which they are able to distinguish in immediately contiguous areas three infarcts, one of which they class as being seven to nine days old, the second eleven to fourteen days and the third twenty-one to twenty-eight days old; and on their case No. 20, in which one infarct of three to four weeks is distinguished from one of four to five weeks; and on their case No. 26, in which in a small infarct they can again distinguish three different ages. The basis for this aging is the method outlined by Mallory *et alii* (1939). Mallory, of Boston, would be proud of his Manchester disciples! Mallory's very fine work of histopathology is not a reliable guide except in those cases (and they do not constitute a majority) in which the infarct is in the bulk a relatively homogeneous mass (usually transmural) of necrotic or partly necrotic muscle. Any pathologist who has seriously attempted to age all of his infarcts according to Mallory's criteria is very well aware of what the latter himself heads as "discrepancies" (*loco citato,* page 666).

Thus, where Blumgart *et alii* have perhaps overstated their case as to the number of occlusions relative to infarcts, Snow *et alii* would seem to have likewise overstated their case as to the number of infarcts relative to occlusions. They found in 25 cases 59 infarcts (2·4 per case). Apart from all of this I object that it is a misleading imputation to state that Blumgart *et alii* reported that in their series there were 53 main artery occlusions associated with 16 infarcts. It is a falsehood to state that Blumgart *et alii* "claimed that occlusion of a main coronary artery occurred very frequently in man without any corresponding myocardial infarct" (Snow *et alii, loco citato,* page 507). The American workers stated no such thing. They discuss the matter with many qualifications on pages 77 to 82 of their article. They stress the fact on page 71 that "the rate at which collateral circulation can develop would seem from the studies to be slow". Nowhere do they abstract the figures quoted by Snow *et alii* and "Current Comment", and in their three pages of "Summary and Conclusions" in sections 5, 10 and 13, which are relevant, the adverb used to qualify the verb in discussing the relationships between occlusion, collaterals and infarction is never "frequently", much less "very frequently". They use the terms "may compensate", "do not necessarily", "may be obviated" in the three respective sections. Any doubts that Snow *et alii* had about the findings of Blumgart *et alii* could have been clarified by reference to their further and long-published works (Blumgart *et alii,* 1950*a*; Blumgart *et alii,* 1950*b*; Zoll *et alii,* 1951).

Further, it is surely an exaggeration to state that clinicians believe that main vessel occlusion is frequently not followed by infarction, and an even greater exaggeration to suggest that pathologists accept main vessel occlusion without infarction as a common event. I suggest that the majority of pathologists (at least when they are not theorizing, but when confronted with the problem in the autopsy room) worry more about the existence and site of the occlusion rather than the absence of an infarct. "Current Comment" further implies that "many recent text-books of cardiology and pathology" have promulgated the supposedly false conclusions of Blumgart *et alii*. A study of Friedberg, Wood, White, Levine, Anderson, Muir, Cecil, Price, Davidson and Harrison does not bear this out. None of these refer to this as a supposedly "frequent" association.

I have made a study of this injection technique as it reveals the pathology in about 150 hearts, about 50 of which show infarcts. I have not been able to endorse all that Blumgart *et alii* have found, but my findings are not very much at variance with theirs. I have made serial slices, as Snow *et alii* have done, and have studied the altered myocardial histology. My own conclusions are not at great variance with that of Snow *et alii* either. I believe that both of the published works have very great value. I do not see the contradiction between the two. My main criticism is directed, however, not toward the Manchester workers but towards you, sir, on these grounds:

1. You have quoted in a subeditorial capacity criticism contained in one article of another without apparent serious reference to the original which was criticized. This is, I submit, to be deplored in any serious publication—and yet not uncommon in both British and American literature.

2. You have equated two studies which, I submit, judged by present publications, are not truly on the same level.

3. You have therefore concluded that because the conclusions of Snow *et alii* "differ considerably from the widely accepted findings of Blumgart, Schlesinger and Davis" you decide to "throw the matter into the melting pot again". You state that the view of Snow *et alii* is "a return to the traditional view, which the work of Blumgart and his colleagues had upset". I submit that this is reactionary in its bad sense. The American workers upset no traditional view. They qualified certain beliefs which had before been tentatively held and which even now, sixteen years after their work, are not yet completely elucidated. Your judgement could well set thought in this country with regard to this matter back just those sixteen years. It is in an endeavour to prevent this and to reach the same reading public that "Current Comment" attracts that I venture at such length to use the correspondence columns (see reading habits of the readers of the journal in "Medical Education" (1955), in which in discussing "Current Comment", its editorial status and its appeal to your readers, Dr. Anderson refers to the powerful influence of your editorial chair).

4. You have aggravated a tendency noticeable in British journals to regard (in metaphorical terms) the Atlantic as the barrier between the Government and the Opposition. This is particularly noticeable in the literature on the broader subject of arteriosclerosis, where works such as Duguid are almost equated with the sum of others such as Cowdry, Aschoff, Keys, Goffman, Hueper, Winternitz, Leary *et cetera*.

Finally, sir, the obvious criticism of my attitude is to remark: "Why does he not publish his own findings instead of writing long letters?" I have not done so previously because I have believed for some time that with such a study it is necessary to publish one's protocols, and because I would require such space as Blumgart *et alii* were fortunately able to command. Experience of this misinterpretation despite the publication of all relevant details leaves me in a dilemma—and you, sir, no doubt exhausted.

Yours, etc.,

F. X. GARVAN HURLEY.

Department of Pathology,
Saint Vincent's Hospital,
Melbourne.

February 24, 1956.

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ALCOHOLISM—A COMMUNITY RESPONSIBILITY.

SIR: May I beg leave to thank Dr. Cade for his most timely paper "Alcoholism—A Community Responsibility".

I think that he will not mind if, with respect, I venture to comment on certain of his points, in the hope of adding to the stimulus he has given for the tapping of the vast amount of knowledge and experience of this subject which must exist in the minds of so many of us who are concerned with mental health.

I should very much like to know by what criteria Dr. Cade considers alcoholism the main ætiological factor in so many of his admissions (35% to 40%). In a given case of psychosis, who drinks, I have usually found it exceedingly difficult, even with very full clinical, personal and social histories, to decide where to place alcohol in the list of other causative factors—particularly of the psychogenic nature—which have been discovered.

It is so easy to fall into the ancient fallacy of *"post hoc ergo propter hoc"*.

Apart from the well-defined class of psychiatric disorders directly due to alcoholism listed in every text-book on mental diseases, how often can we say with certainty: If this patient had never taken alcohol he would not now be suffering from a psychiatric illness? Alcoholism is surely a chronic toxæmia and, as such, very prone to produce mental illness by direct damage to the "organ of thought".

It also produces the phenomenon of addiction. In my view this state is much more complex than the craving for alcohol—or other toxic substance—that it is usually considered to be. Nor can our old friend the conditioned reflex satisfactorily explain it—or the difference between habituation and addiction.

The work being done at the Burden Neurological Institute, Bristol, on this subject and published in *The British Journal of Addiction*, Volume L, Number 2, July, 1953, is, I believe, exceedingly valuable. Permit me to quote the following from it (pages 111-112):

> We no longer ask why, since those people have the choice between good and evil, do they choose evil. We do not ask why they are not better than they are, but what it is about them that is different. . . . From this standpoint alcoholic addiction would be placed in the category of diseased states. This is the new wind which has blown during the last few years, and it accounts for the present increasing world-wide activity in investigations aimed at a better understanding of alcoholism.

Yours, etc.,

R. STEWART KENNEDY,
Consultant (Psychological Medicine).
Repatriation Commission Headquarters,
Melbourne,
March 5, 1956.

THE BRITISH MEDICAL ASSOCIATION AND ITS MEMBERS.

SIR: The honour and dignity of our profession have been suffering a great deal recently as a result of ill-considered publicity in the Press. It is truly surprising that a confidential letter circulated to members of our Association should have been given to the daily papers. It is still more surprising that a detailed account of a meeting of a local association should have appeared in the newspapers. One cannot believe that the local association wished to attack the State Council through the columns of the daily Press, so one must assume that it was done by some irresponsible individual.

I believe that members of our Association, whether they attend meetings or not, have the following obligations to

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MARCH 10, 1956.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	12(4)	4(3)	5(2)	1	..	..	..	..	22
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	1	..	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	15(14)	27(27)	7(5)	..	..	..	..	..	49
Diphtheria	2(1)	2(2)	..	..	2(1)	..	..	..	6
Dysentery (Bacillary)	..	1(1)	4(4)	..	2	..	..	..	7
Encephalitis	2	1	..	3(2)	..	..	..	..	6
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	137(80)	78(49)	..	47(29)	3(1)	..	5	6	276
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	3	..	..	..	3
Leptospirosis	1	..	5(1)	..	..	..	..	..	6
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	1	3(3)	..	..	..	1(1)	..	..	5
Ophthalmia	..	..	..	..	1	..	..	..	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	10(2)	6(4)	4(3)	4(2)	11(4)	2	..	..	37
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	25(15)	..	2	2(2)	..	..	..	29
Salmonella Infection	..	..	..	1	..	..	..	..	1
Scarlet Fever	16(5)	5(4)	5(3)	5(3)	2(2)	..	..	..	33
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	1(1)	..	..	..	1
Trachoma	..	..	..	..	1	..	..	..	1
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	24(12)	17(15)	7(2)	2(2)	6(3)	6(2)	4	..	66
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus)Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

their profession. Firstly, one should carry out one's work efficiently and sympathetically. Secondly, one should elect a strong and truly representative Council and should support it in public. Finally, one should criticize the Council, when criticism is needed, in a proper manner, through the correspondence columns of our own journal and not through foolish and undignified communications to the Press.

Yours, etc.,

IAN S. COLLINS.

Marrickville,
New South Wales,
March 12, 1956.

Notice.

BRITISH MEDICAL ASSOCIATION: NEW SOUTH WALES BRANCH.

Result of Council Election.

THE following members have been elected to the Council of the New South Wales Branch of the British Medical Association for the period 1955-1956 (the number of votes is shown in parentheses):

Representative of Women Members: Dr. Clair Isbister (1021).

Representative of Public (Government) Medical Service Members: Dr. L. W. Wing (915).

Representatives of Country Local Associations: Dr. B. A. Cook, Dr. J. P. Lyttle (both unopposed).

Representatives of Metropolitan Local Associations: Dr. K. S. Jones, Dr. C. R. M. Laverty (both unopposed).

Representatives of the General Body of Members: Dr. M. S. Alexander (1081), Dr. K. C. T. Rawle (1069), Dr. A. J. Murray (1050), Dr. E. S. Stuckey (1038), Dr. A. W. Morrow (1017), Dr. R. H. Macdonald (970), Dr. T. Y. Nelson (956), Dr. D. A. Warden (935), Dr. B. T. Edye (925), Sir Charles Bickerton Blackburn (892), Dr. P. A. Tomlinson (846), Dr. Hugh C. Barry (841), Dr. G. L. Howe (834), Dr. T. M. Clouston (824), Dr. J. A. Paul (813), Dr. D. A. Brown (788).

Medical Appointments.

Dr. B. W. Royall, Dr. L. Vout and Dr. B. E. Welton have been appointed Quarantine Officers (all ports), pursuant to the provisions of the *Quarantine Act*, 1908-1950.

Dr. H. W. Stockley has been appointed Quarantine Officer, Port Adelaide, pursuant to the provisions of the *Quarantine Act*, 1908-1950.

Congresses.

INTERNATIONAL CONGRESS OF CLINICAL CHEMISTRY.

THE International Congress of Clinical Chemistry is to be held from September 9 to 14, 1956, at the Hotel New Yorker, New York City, United States of America. The programme of the Congress will have as its principal topic "The Significance of Metabolic Systems in Clinical Chemistry". Morning sessions will be devoted to reviews of selected subjects by invited speakers, mainly from overseas, and afternoon sessions to contributed papers. Abstracts of the latter should be sent to the Chairman of the Scientific Programme, Dr. Harry Sobotka, The Mount Sinai Hospital, New York 29, New York, before May 15. Exhibits of scientific interest are to be an important feature; arrangements should be made with Dr. Charles L. Fox, New York Medical College, Fifth Avenue and 105 Street, New York 29, Chairman of the Scientific Exhibits Committee, also before May 15. Entertainment will include a reception, trips to points of interest in and around New York, and a Congress dinner. Inquiries should be addressed to the Secretary, John G. Reinhold, 711 Maloney Building, University of Pennsylvania, Philadelphia 4, Pa., United States of America.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Cole, David Ian, M.B., B.S., 1955 (Univ. Sydney), 80 Marsden Street, Parramatta, New South Wales.

Thomas, Edna Rae, M.B., B.S., 1955 (Univ. Sydney), 29 Gibbons Street, Auburn, New South Wales.

Holmes, Vera, M.B., B.S., 1943 (Univ. Durham), Wakefield Gardens, Ainslie, Canberra, A.C.T.

Golomb, Minna, M.B., B.S., 1954 (Univ. Sydney), 3-251 Old South Head Road, Bondi, New South Wales.

Ferguson, Peter Langbene, M.B., B.S., 1955 (Univ. Sydney), Royal Newcastle Hospital, Newcastle, New South Wales.

England, Theodora Margaret, M.B., 1925 (Univ. Sydney), Ch.M., 1954 (Univ. Sydney), D.P.M. (Sydney), 1938, Kenmore Mental Hospital, via Goulburn, New South Wales.

Farrell, John Caldwell, M.B., B.S., 1954 (Univ. Sydney), 50 Chesterfield Parade, Waverley, New South Wales.

Diary for the Month.

APRIL 3.—New South Wales Branch, B.M.A.: Organization and Science Committee.

APRIL 4.—Western Australian Branch, B.M.A.: Branch Council.

APRIL 6.—Queensland Branch, B.M.A.: General Meeting.

APRIL 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 8 King's Park, West Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

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